表 1　RVH 疑診の度合い[2]

A）低い（<1%）：さらなる検査必要なし
RVH/RAS を疑わせる所見のない中等症までの高血圧
B）中程度（5〜15%）：RVH/RAS の非侵襲的検査の適応
・重症高血圧（DBP＞120 mmHg） ・治療抵抗性高血圧 ・20 歳未満あるいは 50 歳以上で持続性の中等症一重症高血圧が急に出現した場合 ・以下のいずれかの症候を持つ中等症高血圧（DBP＞105 mmHg）：喫煙，他の動脈に閉塞所見がある，原因不明の血清クレアチニン上昇 ・ACE 阻害薬で血圧が正常化した中等症あるいは重症の高血圧：特に，喫煙者あるいは最近発症した高血圧の場合（ただし，ACE 阻害薬で血圧が下降しないことは RVH の除外にはならない）
C）高い（>25%）：腎動脈撮影の適応
・重症高血圧（DBP＞120 mmHg）で進行性腎機能低下を伴ったり，積極的治療に抵抗性の場合（特に，喫煙者あるいは他の動脈に狭窄病変を伴う症例） ・加速型高血圧あるいは悪性高血圧（grade Ⅲ-Ⅳの高血圧性網膜病変） ・腹部血管雑音（持続性，高ピッチで腎動脈の領域に限局する） ・直近のクレアチニン上昇を伴う高血圧でクレアチニン上昇の原因が不明な場合や ACE 阻害薬によるクレアチニン上昇 ・中等症一重症高血圧で腎のサイズに左右差がある

表 2　RVH の非侵襲的診断法の選択

診断法	特徴	選択の有無
末梢 PRA	RVH の 50%でのみ高値	なし
Captopril 負荷 PRA	報告により sensitivity や specificity に差異	なし
腎静脈 PRA	Sensitivity が低い	なし
Rapid-sequence IVP	Sensitivity が低い 造影剤の量が多い	なし
アスピリン（カプトプリル）・レノグラム	研究者によっては first-choice，sensitivity に差異 腎障害例では診断精度低い	一部あり
超音波ドップラー	腎機能障害で影響されない 施設によっては好成績 技術に成熟が必要	一部あり
CT angiography	Sensitivity 高いが specificity 低い MRA よりも副動脈の検出度が高い 腎不全例では造影剤の投与が問題	一部あり
MR angiography	診断精度が高い 副動脈の検出度が低い 腎機能障害例にも使える	あり

RAS 以外に食塩摂取量，体位，降圧薬などによっても影響を受け，本態性高血圧の約 20%でレニンが高値になる。それ故，RVH の診断に末梢血レニンはあまり役立たない。

1）Captopril レノグラム[3]（Aspirin レノグラム[4]）

^{99m}Tc-diethylenetriamine pentaacetic acid (DTPA) は糸球体濾過量の測定に利用されるのに対し，^{131}I-orthoiodohippurate や ^{99m}Tc-mercaptoacetyltriglycine (MAC) は腎血漿流量を反映する。いずれの核種を使用したレノグラムでも RAS に基づく血行動態の変化が観察できる。有意の RAS により，環流圧が低下し血流は減少するが，angiotensin II の上昇により輸出細動脈は収縮するため，糸球体濾過は維持される。ACE 阻害薬により狭窄側輸出細動脈の収縮が解除され，糸球体内圧が低下する。その結果，狭窄側で糸球体濾過量が低下し，RI の取込みや分泌は抑制される。以上の機序により RAS では ACE 阻害薬投与後にレノグラム上の左右差が増強される。captopril レノグラムの sensitivity は報告によって異なり，70〜90%とされる。specificity も同様に高い値を示す。

Aspirin レノグラムは captopril と同様の診断的意義を持つ。RAS が疑われた 75 例に両方の検査を施行した成績では診断精度に差を認めていない[5]。プロスタグランジンは腎虚血によるレニン分泌のメディエーターである。Aspirin はプロスタグランジン産生の抑制を介して狭窄腎からのレニン分泌を阻害する。その結果，狭窄腎のレニン・アンジオテンシン系は抑制され，腎血行動態は ACE 阻害薬による場合と同様の影響を受けることとなる。**図 1** に aspirin 負荷によりレノグラムの左右差が明瞭になった 1 例を示す。

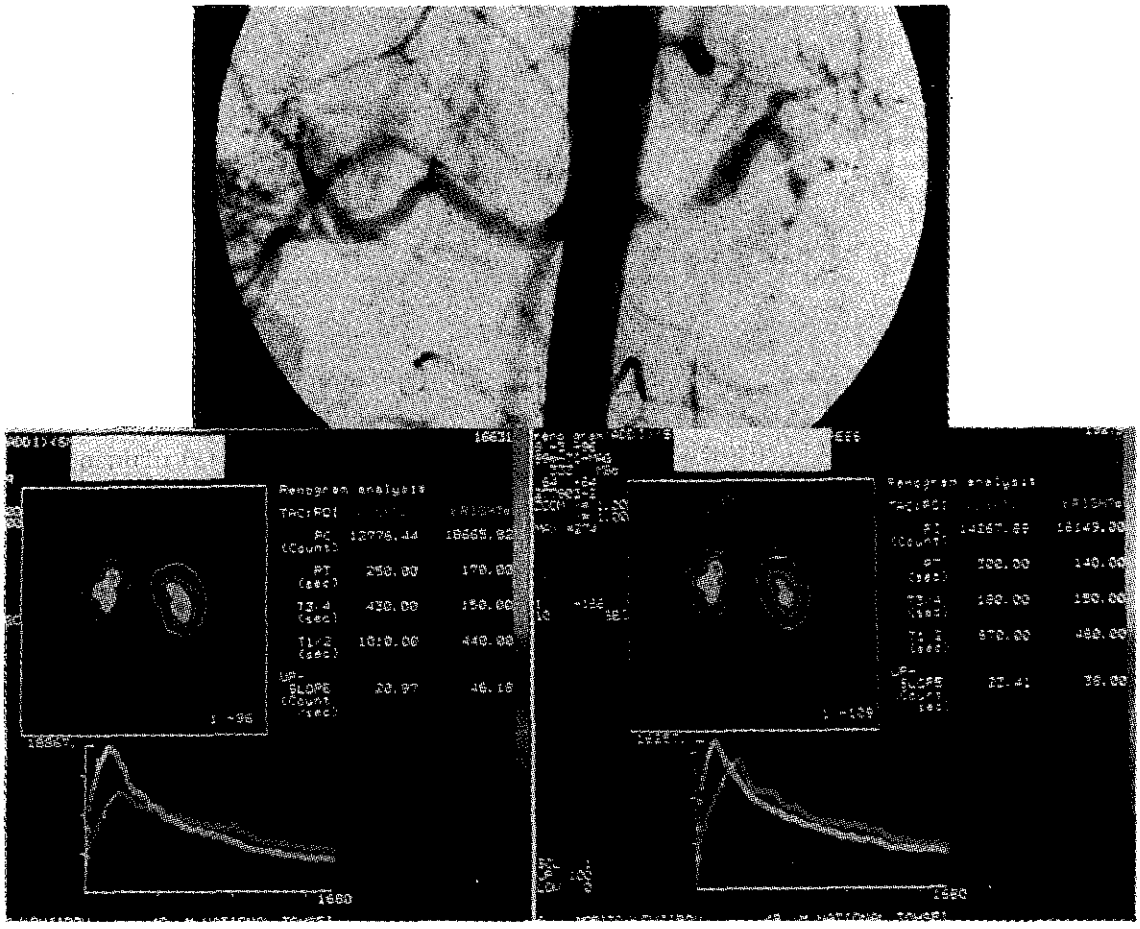

図 1　左腎動脈主幹部狭窄におけるアスピリンレノグラム

下段左図は^{99m}Tc-DTPA を用いた通常のレノグラム，右図はレノグラム検査 1 時間前にアスピリンを 20 mg/kg 経口した場合のレノグラム。アスピリン投与後には左腎レノグラムのピークが右方に移動し左右差が明瞭になった。

2）超音波ドップラー法[6]

超音波 B モード法とドップラー法を組み合わせることにより，腎動脈と腎実質を画像化し，血流速度が測定できる。検査前に降圧薬を中止する必要がない，両側 RAS 例でも診断精度が落ちない，腎機能障害の程度によって影響を受けない，などの利点がある。短所としては技術的習熟が必要であることや時間がかかることなどがある。90%以上の診断精度を報告している施設がある一方，sensitivity 70%前後とする報告もある。かなりの例で血流シグナルの検出ができず診断不能なことも短所となる。

3）MRA[7]

Gadolinium enhancement により血管内の緩和時間を短縮し，乱流部位でのシグナル脱落を防止できる。また，通常の造影剤と異なり，Gadolimium には殆ど腎毒性がない。本法により精度の高い腎動脈 MRA が可能となった。現在 MRA の空間分解能は 2～2.5 mm であり，腎動脈主幹動脈の評価には十分である。**図 2** に MRA により描出できた RVH の 1 例を示す。一方，腎動脈副動脈の管径は 1～3 mm であり，画像化するには不十分である。腎動脈主幹部における MRA の診断精度は極めて優れている。Conventional angiography を standard とした場合，sensitivity 95%以

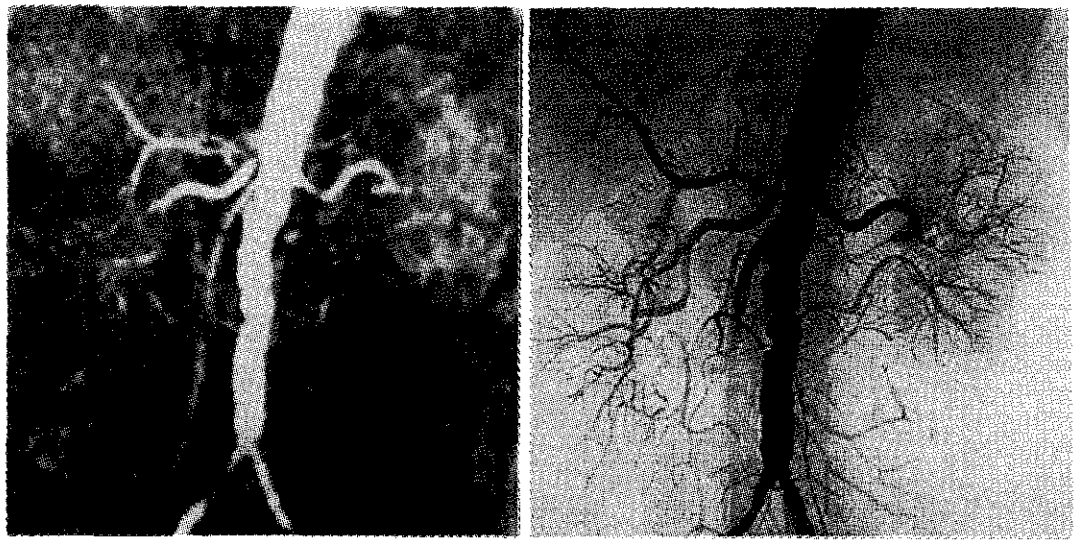

図 2　右腎動脈主幹部狭窄による腎血管性高血圧例における DSA と MR angiography
MR angiography（左図）でも DSA（右図）と同様腎動脈主幹部狭窄が描出されている。

上，specificity 90%以上とされる。一方，副動脈の sensitivity は 90%未満である。また，腎動脈分枝に病変を生じる FMD では無効の場合があるので留意する。MRA の利点として解剖学的情報以外に，狭窄病変が血行動態へ及ぼす影響も評価できることがあげられる。Gadolinium が主に糸球体濾過によって排泄されることを利用して，MRA renography を行うことも可能となった[8]。

III. RVH の治療

RVH では降圧により高血圧の合併症を予防するとともに，腎機能を保持することも重要な課題となる。治療手段としては，PTRA，ステント挿入術，外科的手術，薬物治療がある。血行再建術により，血圧が正常化しない場合でも，血圧下降や降圧薬の減量などが期待できる。FMD による RVH では血行再建術が第 1 選択となるが，粥状動脈狭窄症に対する血行再建術の意義については，各症例について検討を要する。

1．薬物療法

ACE 阻害薬や AII 受容体拮抗薬を 1 腎 1 クリップ型や 2 腎 2 クリップ型の RVH に投与した場合，可逆性急性腎不全をきたすことがある。以上の例では ACE 阻害薬の投与は禁忌とされる。これらの例の降圧には，利尿薬，β 遮断薬，Ca 拮抗薬などを用いる。降圧や ACE 阻害薬により腎機能低下に陥る高度 RAS 例では血行再建術により腎機能の保持を図る。

表 3　PTRA による降圧効果（病因別）

	例数	拡張成功例数（%）	降圧効果			有効率（%）
			正常化（%）	改善（%）	不変（%）	
FMD	24	23 (95.8)	9 (37.5)	13 (54.2)	1 (4.2)	91.7
動脈硬化	20	17 (85.5)	6 (30.0)	7 (35.0)	7 (35.0)	65.0
外傷	1	1 (100)	1 (100)	0	0	100
計	45	41 (91.1)	17 (37.7)	20 (44.4)	8 (17.8)	82.1

（追跡期間　3 カ月～6 年 8 カ月）

2．血行再建術

1）PTRA

PTRA は外科治療に比較し，全身麻酔が不要なこと，入院期間が短いこと，繰り返しが可能なことなどが利点となる。合併症はまれであるが，造

影剤による腎不全，コレステロール塞栓，腎動脈の破裂や解離，腎動脈血栓，仮性動脈瘤，血腫などがある。FMDに対するPTRAの成功率は90%以上，非入口部の粥状動脈硬化でも70～90%と良い成績が得られている。私どもの以前の成績（表3[9]）でも，FMDにおいてはPTRAの成績が良好であることが確認されている。しかし，入口部狭窄ではPTRA直後にelastic recoilを起こしやすく，30～60%の成功率に留まる。さらに，長期の再狭窄率も高くなる。

PTRAによる降圧の評価は，血圧が149/90 mmHg未満に下降し降圧薬が不要になった場合は“治癒”，降圧薬が減量になった場合や10～15%の降圧が得られた場合は“改善”と判定される。1990年度のreview[10]では“治癒”あるいは“改善”と判定される割合は粥状動脈硬化症70%，FMDで92%であった。最近，粥状動脈硬化によるRVH 106例を薬物治療群とPTRA群の2群にランダム化してPTRAの予後に関する前向き研究の結果が報告された[11]。12カ月間追跡したIntention-to-treat解析によると，両群間で血圧，降圧薬の投与量，腎機能には差を認めなかったことより，PTRAは薬物治療より優れているとは言えなかった。動脈硬化症によるRVHでは，PTRAは3種以上の降圧薬の併用にもかかわらず高血圧が持続する場合や，進行性RASの場合に限定されるべきであると結論している。

2）腎動脈ステント

入口部病変では技術的成功率が低く，バルーン拡張術の代わりにステント挿入術が勧められる。最近では，より末梢の病変にもステント術が施行されるようになった。ステント術による開存率は入口部で95～100%[12]，末梢病変でも同様の成績が得られている。再狭窄率は報告によって異なるが，PTRAよりは低い[13]。

ステント挿入術の降圧効果については開存例の40～70%で“治癒”または“改善”の成績が得られている。腎機能については改善26%，安定48%，悪化26%との成績が得られている。

入口部狭窄に対するPTRAとステント挿入術の前向きランダム化比較試験[14]では，初期成功率（PTRA　57%，ステント88%），6カ月開存率（PTRA 29%，ステント75%），再狭窄率（PTRA 48%，ステント14%）とステント群で明らかに良好な結果が得られた。

3）外科手術

RVHの外科治療として腎動脈バイパス術，片側腎摘出術，体外腎血管形成術，内膜除去術，アテレクトミーなどがある。これらのうち，バイパス術の頻度が最も多くなる。成功率は高く，手術死亡率6%，再狭窄率は10%未満である[13]。高血圧に対する効果は非常に良好で，60～90%の例で“改善”または“治癒”の結果が得られている。腎機能障害進行への効果も良好な成績が得られており，80%以上の症例で改善あるいは安定するとの結果が得られている。

おわりに

FMDによるRVHの治療方針はほぼ定まっている。一方，動脈硬化性RASは全身の動脈硬化を伴うことが多いことから，血行再建術を行った場合の降圧効果や予後については一定の結論を得たとは言い難い。今後，多数例についての比較試験により再建術の意義を評価する必要がある。最後に，動脈硬化のリスクを治療することは血行再建術の有無に拘らず不可欠であることを追記したい。

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C-reactive protein's effect on carotid artery atherosclerosis

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The development of atherosclerosis is thought to be partly caused by an inflammatory response. Of the circulating markers related to inflammation, high-sensitivity C-reactive protein has the most consistent relationship to the risk of cardiovascular disease events in a variety of clinical settings.[1] Few longitudinal studies have been done, however, to determine the relationship between the development of atherosclerotic lesions and high-sensitivity C-reactive protein concentration.[2,3] Little clinical evidence shows that an elevated high-sensitivity C-reactive protein concentration results in the development of atherosclerosis.

Carotid artery atherosclerosis is closely related to the presence of cardiovascular disease and the risk of cardiovascular events.[4] We sought to determine the relationship between high-sensitivity C-reactive protein concentration and the development and severity of carotid artery atherosclerosis.

Patients and methods

One hundred ninety-one outpatients ages 40 to 79 years were examined for carotid artery atherosclerosis because they had risk factors for cardiovascular disease. At the baseline examination, blood samples were collected for the measurement of high-sensitivity C-reactive protein concentration. High-resolution B-mode ultrasonography was performed repeatedly over a period of at least 2 years to evaluate carotid artery atherosclerosis. Because the upper limit of normal for the intima-media thickness is 1.0 mm, lesions with a focal intima-media thickness of 1.1 mm or greater were defined as atheromatous plaques. We calculated the plaque score by summing all of the plaque thickness measurements in both carotid arteries.[5] The plaque number and plaque score were used to estimate the severity of carotid artery atherosclerosis. We estimated the development of atherosclerosis by determining the change in plaque number and plaque score per year (the last value minus the baseline value, divided by the number of follow-up years). Patients with a plaque score above 10.0 were not enrolled.

Time-saver

We examined the relationship between baseline high-sensitivity C-reactive protein concentration and carotid artery plaques in 179 patients ages 40 to 79 years who had traditional risk factors for cardiovascular disease. The log-transformed high-sensitivity C-reactive protein concentration was related to the progression of carotid artery atherosclerosis after adjusting for traditional risk factors ($p < .001$). Our results suggest that a therapeutic strategy for decreasing high-sensitivity C-reactive protein concentration may be valuable for preventing the development of carotid atherosclerosis. ♥

TABLE 1

Association between atherosclerosis risk factors, baseline plaque score, and change in plaque score per year

	Baseline plaque score	Change in plaque score/year
Risk factors		
Age (years)	0.288*	0.04
Men	3.1 ± 3.0	0.75 ± 1.12
Women	2.0 ± 2.1†	0.39 ± 0.92*
Medical history		
Hypertension		
Yes	2.7 ± 2.6	0.61 ± 1.12
No	2.2 ± 2.6	0.46 ± 0.81
Blood pressure (mm Hg)		
Systolic	0.192*	0.101
Diastolic	0.006	−0.066
Statins		
Yes	2.7 ± 2.4	0.50 ± 0.95
No	2.5 ± 2.7	0.60 ± 1.06
Diabetes		
Yes	3.8 ± 2.5	0.53 ± 1.17
No	2.3 ± 2.6	0.57 ± 1.01
Smoker		
Current	2.8 ± 2.6	1.04 ± 1.52
Noncurrent	2.5 ± 2.6	0.52 ± 0.94
Cigarette pack-years	0.204*	0.108
Cardiovascular disease		
Yes	3.2 ± 3.1	0.69 ± 1.19
No	2.3 ± 2.4	0.53 ± 0.96
Laboratory measures		
Total cholesterol (mg/dL)	0.105	0.21
HDL cholesterol (mg/dL)	−0.085	−0.007
Fasting blood glucose (mg/dL)	0.227*	0.18†
Glycosylated hemoglobin (%)	0.256*	0.084
High-sensitivity C-reactive protein (mg/dL)	0.227*	0.268*

The values shown are correlation coefficients for measured risk factors and mean ± SD for categorized risk factors. The Spearman rank correlation test was used for measured risk factors and the Mann-Whitney *U* test was used for categorized risk factors.
*$p < .01$, †$p < .05$.

We performed multiple linear regression analyses to assess the contribution of high-sensitivity C-reactive protein concentration compared with the contribution of traditional risk factors to the prediction value of each measure of atherosclerosis. Log-transformed high-sensitivity C-reactive protein values were used in the model.

Results

Of the 191 screened patients, 179 were enrolled in the study. Hypertension, hypercholesterolemia, and diabetes mellitus were observed in 72%, 43%, and 14% of the patients, respectively, and were being managed by medication at study entry. At baseline, the plaque number and plaque score were 1.6 ± 1.6 (median, 1.0) and 2.6 ± 2.7 (median, 1.7), respectively. Several measured traditional risk factors, as well as high-sensitivity C-reactive protein concentration, significantly correlated with the severity of baseline carotid artery atherosclerosis (TABLE 1). Based on multiple linear regression analysis using baseline values, high-sensitivity C-reactive protein concentration did not significantly correlate with the plaque number or score after adjusting for age, sex, hypertension, hypercholesterolemia, diabetes mellitus, and cigarette pack-years (TABLE 2).

We evaluated the relationship between different tertiles of high-sensitivity C-reactive protein concentration and the change in plaque number and plaque score per year (FIGURE). Change in plaque number and score per year were significantly greater in patients in the highest tertile than in those in the middle and lowest tertiles. High-sensitivity C-reactive protein concentration correlated with the change in plaque number and score per year on simple regression analysis. This correlation was stronger than for measured traditional risk factors and remained significant after adjust-

TABLE 2

Association between high-sensitivity C-reactive protein concentration and measures associated with carotid artery atherosclerosis

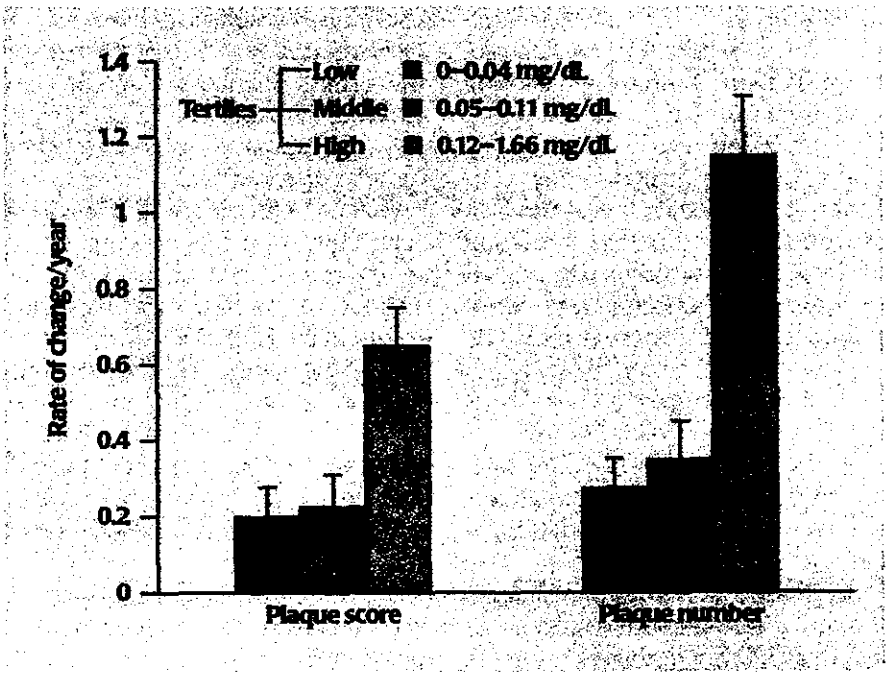
	Simple regression		Multivariate regression	
All patients (N = 179)				
Plaque number	0.217	$p = .003$	0.113	
Plaque score	0.227	$p = .002$	0.110	
Change in plaque number/year	0.223	$p = .003$	0.289	$p < .001$
Change in plaque score/year	0.268	$p < .001$	0.296	$p < .001$
Change in plaque score/year/subgroup				
Men (n = 89)	0.381	$p < .001$	0.325	$p = .004$
Women (n = 90)	0.223	$p = .036$	0.252	$p = .019$
Noncurrent smokers (n = 158)	0.265	$p = .022$	0.269	$p = .003$
No statin therapy (n = 136)	0.278	$p = .001$	0.283	$p = .002$
No cardiovascular disease (n = 128)	0.209	$p = .019$	0.234	$p = .013$
Patients with preexisting carotid plaque (n = 123)				
Change in plaque number/year	0.324	$p < .001$	0.324	$p = .001$
Change in plaque score/year	0.368	$p < .001$	0.332	$p = .001$

ing for traditional risk factors and the severity of baseline carotid artery atherosclerosis (TABLE 1). In the subgroup analysis, the association between high-sensitivity C-reactive protein concentration and change in plaque score per year remained significant after adjusting for traditional risk factors (TABLE 2).

Discussion

Few researchers have reported on the association between C-reactive protein concentration and the development of carotid artery atherosclerosis. The results of cross-sectional studies showed no association between high-sensitivity C-reactive protein concentration and severity of carotid artery atherosclerosis.[6,7] In a prospective study, Sander and colleagues found that patients with high C-reactive protein levels (≥ 0.5 mg/dL) and *Chlamydia pneumoniae* seropositivity had the largest progression of early carotid artery atherosclerosis.[3]

FIGURE



Mean change in plaque score and plaque number per year according to tertiles of high-sensitivity C-reactive protein concentration. Changes were significantly greater in patients in the highest tertile of baseline C-reactive protein concentration than in those in the middle and lowest tertiles ($p < .05$, one-way analysis of variance with the Bonferroni correction).

The results of our cross-sectional analysis of baseline values showed no significant association between C-reactive protein concentration and carotid artery atherosclerosis after adjusting for traditional risk factors. We showed, however, that high-sensitivity C-reactive protein concentration independently predicts the development of early carotid artery atherosclerosis. It appears to be a marker for inflammation that is related to the rate of plaque development rather than to the extent or severity of plaque burden.

Atherosclerosis development accelerated with increasing high-sensitivity C-reactive protein levels, even when the values were within the normal range. This finding links C-reactive protein to the early processes of atherosclerosis as well as to the late processes of the disease, which lead to cardiovascular events. This finding may also support the hypothesis that C-reactive protein directly interacts with atherosclerotic vessels by activating the complement system, thereby promoting inflammation and thrombosis.[1,8] Accumulating evidence suggests that C-reactive protein may contribute to monocyte recruitment in atherogenesis, monocyte induction of tissue factor, which is potentiated by interferon-gamma and lipopolysaccharide, adhesion molecule expression in human endothelial cells, and macrophage uptake of low-density lipoprotein.[9-12]

Based on the results of our previous study, we defined atherosclerotic plaque as an intima-media thickness of 1.1 mm or greater.[5] The Rotterdam Study suggests that although an intima-media thickness of less than 1.1 mm in the common carotid artery may not represent local atherosclerosis, it may reflect an adaptive response to altered flow, lumen diameter, shear stress, or pressure.[13]

The hazard ratio for cardiovascular disease events is increased for an intima-media thickness greater than 1 mm.[4] Based on this definition, our results show that higher concentrations of high-sensitivity C-reactive protein correlate with increased numbers of atherosclerotic plaques and an increased plaque score. When patients who had preexisting carotid plaques were analyzed separately, we found a stronger correlation, possibly because these patients had started developing atherosclerosis. This idea is supported by the Bruneck Study, which showed a closer correlation between a new inflammatory marker and the progression of carotid artery atherosclerosis in patients with rather than without preexisting plaque.[14]

C-reactive protein concentration, as assessed by the standard procedure, tended to be higher in patients with newly developed plaques than in those without new plaques.[2] We focused on the early stage of carotid artery atherosclerosis for two reasons: it reflects generalized atherosclerosis, and a slight progression significantly increases the prevalence of cardiovascular disease and the risk of a cardiovascular disease event.[4]

Managing traditional risk factors is important, but it does not completely inhibit the development of atherosclerosis or prevent cardiovascular events. In the United States, up to one half of all myocardial infarctions occur in individuals with a low-to-moderate risk of cardiovascular disease based on total cholesterol and high-density lipoprotein (HDL) levels. Our results show that high-sensitivity C-reactive protein concentration predicts the development of carotid artery atherosclerosis, independent of the effects of traditional risk factors.

Conclusion

A therapeutic strategy, such as aspirin or HMG-CoA reductase inhibitor (statin) use, that decreases C-reactive protein levels and inhibits inflammatory response may prevent the progression of atherosclerosis and subsequent cardiovascular events.[1,15] Many studies have used ultrasonography of the carotid artery to estimate the antiatherosclerotic effect of medication.[4] The combined evaluation of high-sensitivity C-reactive protein concentration and carotid artery plaques may be useful to estimate anti-inflammatory drug effects on the progression of atherosclerosis and occurrence of cardiovascular events. ■

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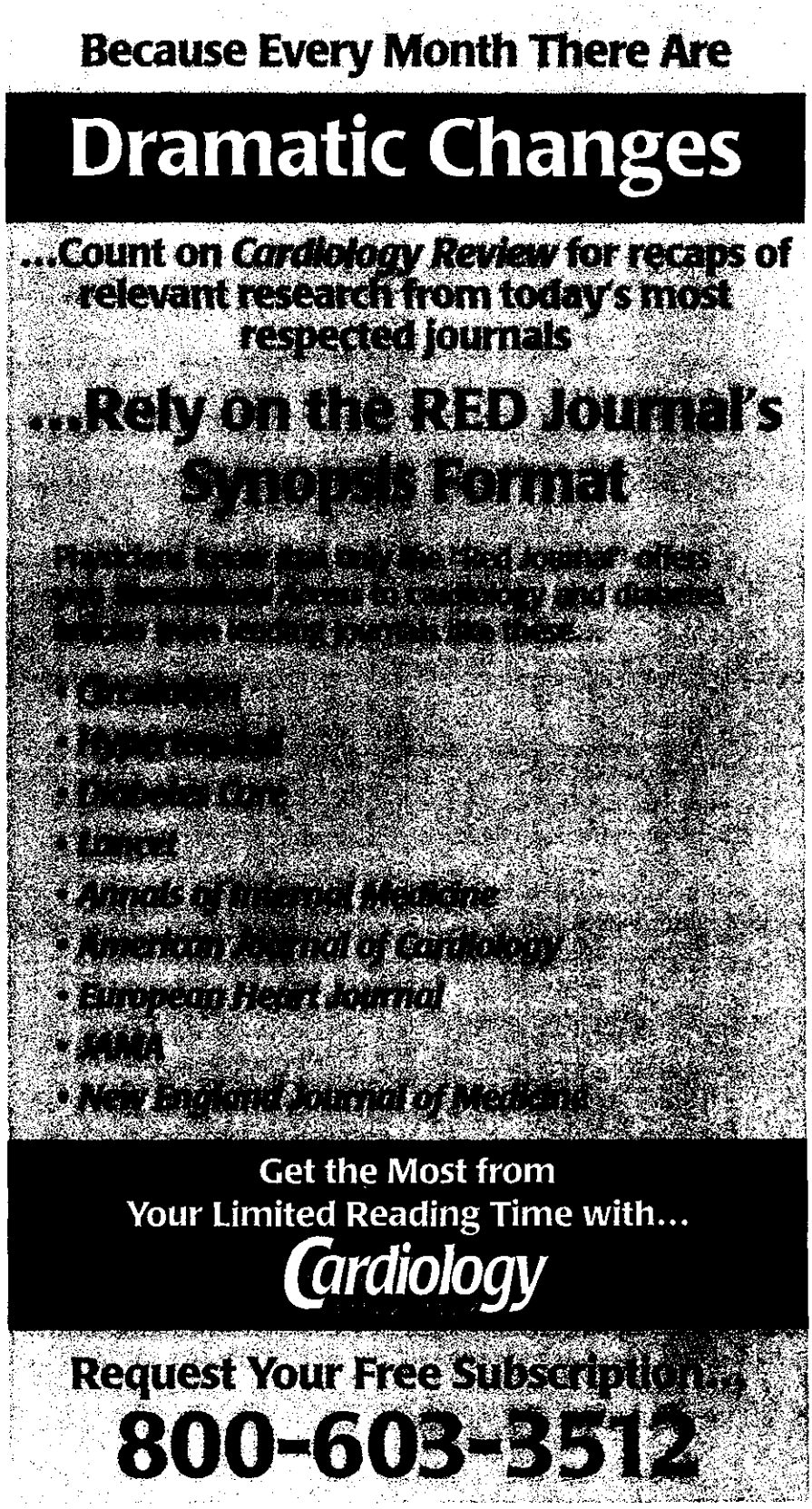
A more detailed discussion of this topic can be found in Hashimoto H, Kitagawa K, Hougaku H, et al. C-reactive protein is an independent predictor of the rate of increase in early carotid atherosclerosis. Circulation 2001;104:63. (TABLES and FIGURE adapted with permission.)



特　集

脳血管障害と高血圧治療

高血圧性脳症の病態診断法の進歩と降圧治療

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◇高血圧性脳症とは，急激な著しい血圧上昇とともに，頭痛，吐き気，霞視（視力障害），痙攣，意識障害などの症状が出現する高血圧緊急症の1つである．近年の画像診断法の進歩により，高血圧性脳症発症の病態が血管腹性浮腫であることを示唆する特徴的な所見が得られるようになった．すなわち，MRI検査において拡散強調画像では病変部位に異常を認めず，みかけの拡散係数は増加することが報告されている．さらに，動揺の所見を子癇発作，免疫抑制薬投与患者などにおいても認めるため，これらの疾患を包括してreversible posterior leukoencephalopathy syndromeという新しい概念も提唱されている．高血圧性脳症はただちに降圧治療を開始すべきである．ただし，重症例では神経細胞性浮腫も合併している可能性があるため，急激な過度の高圧により脳虚血を増強させることがないように，降圧速度，降圧レベルについて注意が必要である．◇

はじめに

従来，高血圧性脳症の病態は，血管攣縮による脳虚血・神経細胞毒性浮腫（cytotoxic edema）説と脳血流自動調節能の破綻による高灌流（hyperperfusion）・血管原性浮腫（vasogenic edema）説の2説が唱えられていた[1]．しかし，MRI画像診断法の進歩によって脳浮腫の超早期から“水”の移動を捉えられるようになり，これを応用した拡散強調画像，みかけの拡散係数（apparent diffusion coefficients；ADC）測定結果が報告され，最近では後者が有力な発症メカニズムと考えられている[2][3]．また，高血圧性脳症およびこれと類似した臨床像，画像所見を呈する疾患（子癇，免疫抑制薬投与患者等）をまとめた新しい概念：可逆性後部白質脳症（reversible posterior leukoencephalopathy syndrome；RPLS）が提唱されており[4]，これらの疾患では拡散強調画像，みかけの拡散係数に関する所見が共通している[2][3][5]（注：病名の解釈の仕方による混乱を避けるために，本稿では血圧上昇のみに起因する場合に高血圧性脳症と定義する）．

高血圧性脳症は，緊急に降圧する必要がある疾患（高血圧性緊急症）の一つとして臨床上重要であり，ただちに降圧治療を開始すればほぼ完治するが，治療が遅れると重篤な状態に陥り致死的なこともありうる．ただし，その鑑別疾患として重要な脳梗塞急性期などでは逆に降圧治療の休止が必要であり，また，高血圧性脳症においても重症例では脳梗塞を発症することもあるため降圧速度，降圧レベルに関しては急激に過度に降圧しないほうがよい場合もあると考えられる．さらにはRPLSでは，血圧上昇が軽度の場合もあり降圧治療以外に各疾患に応じた治療も重要である．

本稿では，高血圧性脳症，RPLSについてこれまでの病態診断に関する報告を整理し，適切な降圧治療方法について考察する．

KEY WORD

高血圧性脳症，RPLS，拡散強調画像，みかけの拡散係数，脳血流自動調節能，血管原性浮腫

1．高血圧性脳症の病態

動物実験では，ネコの脳血管径(抵抗血管である径150 μm以下の軟膜動脈)を直接測定した報告がある[1]．脳血管は，血圧が低下すれば拡張し血圧が上昇すれば収縮するが平均血圧がある限界値（約180 mmHg）を超えると血管内圧に対して血管が耐えられなくなり部分的に拡張し不規則なソーセージ-細ひも（sausage-string）様になり，さらに，びまん性に全体が拡張していくことが観察されている．これにより，血圧変動に対して脳血流を一定に保つ機能である脳血流自動調節能が破綻（breakthrough of cerebral blood flow）して脳血流が増加し，血液脳関門（blood-brain barrier）が障害され，血漿成分が血管周囲へ漏れ出し血管原性脳浮腫を起こし高血圧性脳症を発症する[1]．脳卒中自然発症高血圧ラット（stroke-prone spontaneously hypertensive rats）を用いた実験では，すでに著しい浮腫を示している脳局所では血流が低下しているが，血液脳関門が障害されているもののまだわずかな浮腫しか伴っていない部位の局所脳血流は正常かもしくは上昇していることが報告されている[6]．ヒトにおいても，アンジオテンシンIIを静注し正常血圧者では平均血圧150 mmHgを超えると脳血流自動調節能が破綻し脳血流量が増加することが報告されている[1]（図1）．

本症は短時間にダイナミックに変化するため，発症後の病態について経時変化を画像診断で観察することは難しくヒトにおいてはこれまでに詳細に検討した報告はない．仮説として，血管原性浮腫が進行すると間質圧が上昇し毛細血管を圧迫して微小循環が障害され，その結果，局所脳血流が低下し脳虚血となり神経細胞性浮腫が合併してくると考える報告がある[7]．この際，過度に降圧し過ぎると一見正常血圧にみえても低灌流になっており，重症例では脳梗塞を起こす可能性がある[7]．脳血流を評価したSPECT，MRI脳灌流画像（perfusion）の結果の不一致（**表1**）の原因の一つとして，微小循環障害，神経細胞性浮腫合併の有無が考えられる．

脳血流自動調節のメカニズムについては，神経性，筋原性，代謝性調節説などがある[1]．神経性調節説においては，頸動脈領域よりも椎骨脳底動脈領域の血管のほうが交感神経支配が乏しくその灌流領域の自動調節能が障害されやすいといわれている[8]．最近では，脳幹部のみが障害された症例も数例報告されている．臨床症状は，頭痛（および吐き気），霞視(あるいは皮質盲，視覚障害)，痙攣，意識障害などが特徴的な症状である[8]．

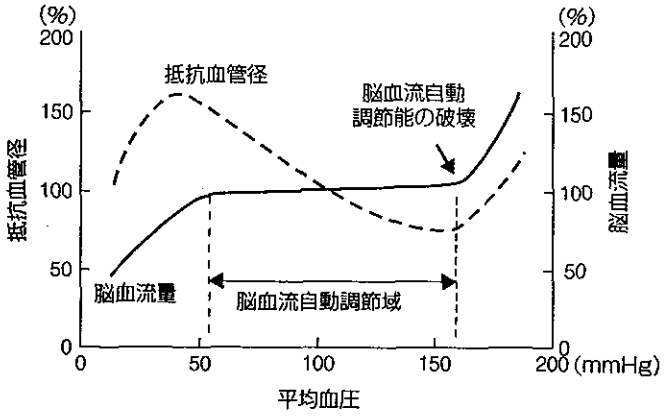

図1．正常血圧者の脳血流自動調節能

2．新しい概念：RPLSについて

1996年にHincheyら[4]により提唱された概念で，SLE，急性腎炎，あるいは肝腎症候群における高血圧性脳症や，子癇，免疫抑制状態(シクロスポリン，インターフェロンα，タクロリムス使用患者）の患者において，前項で示した臨床症状が出現し，画像診断上，大脳半球後部（後頭葉，頭頂葉）を主として，脳幹部，小脳などの椎骨脳底動脈系に，両側性に広範な白質病変を認め，降圧治療，抗痙攣薬投与，免疫抑制薬の中止または減量などにより神経症状が消失する疾患群をまとめたものである．その後の拡散強調画像，みかけの拡散係数を測定した検討では，**表1**に示したような点が脳梗塞とは異なっており新しい概念として注目された．高血圧性脳症，RPLSでは，脳血管の脳血流自動調節能の障害により血管原性浮腫がおこり間質の水の動きが増加し，みかけの拡散係数（ADC）が障害部位において増加すると考えられている．ちなみに神経細胞内ではミトコンドリアなどの小器官を含み，このため水分子の拡散は制限され，細胞外（間質）にくらべ水の動きが少ない（ADCが低い）．脳虚血，脳梗塞早期におけるADCの低下は，神経細胞毒

表 1. 高血圧性脳症，RPLS，脳梗塞の臨床症状，検査所見

	高血圧性脳症	RPLS（高血圧性脳症を除く）	脳梗塞
病態	血管原性浮腫（vasogenic edema）	高血圧性脳症と同じ	神経細胞毒性浮腫（cytotoxic edema）
臨床症状	頭痛（および吐き気），霞視，（あるいは皮質盲，視覚障害），痙攣，意識障害などが特徴的	高血圧性脳症と同じ	脳局所症状が出現するが，霞視，痙攣，頭痛は比較的まれ
血圧	極度の高血圧	血圧上昇していることが多いが軽度の上昇の場合もある	RPLS と同じ
経過	可逆性	高血圧性脳症と同じ	後遺症を残すことが多い
急性期治療	降圧	降圧，あるいは免疫抑制薬の減量，中止など	原則として降圧薬休止
血液検査	報告なし	von Willebrand factor，エンドセリン，フィブロネクチンが上昇（血管内皮細胞の活性化状態を意味する）[10]	種々の報告あり
血管造影，MRA，経頭蓋超音波ドプラ法	報告なし	頭蓋内主幹動脈の攣縮[11)~13)][呈示症例]	狭窄性病変
脳血流 SPECT*	病変部位脳血流増加[14]，	病変部位脳血流増加[15]，低下[呈示症例]	病変部位脳血流低下
MRI			
T_1，T_2強調画像	病変部位高信号	高血圧性脳症と同じ	高血圧性脳症と同じ
フレア画像			
脳灌流画像*（Perfusion）	病変部位の脳血流低下[7)16)]	報告なし	高血圧性脳症と同じ
ガドリニウム造影	報告なし	病変部位増強効果あり[14]	増強効果あり
MRS	報告なし	病変部位で N-acetyl-aspartate/Creatinine 比が低下 Lactate の存在は症例により異なる*[17]	RPLS と同じ Lactate の存在あり
拡散強調画像（diffusion）	病変部位において正常，[3] あるいはわずかに高信号*	高血圧性脳症と同じ[2)3)5)]	高信号
みかけの拡散係数	病変部位において増加[3]	高血圧性脳症と同じ[2)3)5)]	低下

*重症度（脳神経細胞の虚血を合併の有無，程度）により所見が異なる可能性が考えられる．

性浮腫により細胞が膨化し相対的に ADC の低い領域が増加することが一因と考えられている．拡散強調画像では，その算出式に緩和時間，とくに T_2の要素が含まれているため水の動きに起因する変化が相殺され高血圧性脳症の病変部位では正常になると考えられている．

これらは，必ずしも可逆性ではなく病態の項で述べたように重症例では永久的に脳損傷を残すこともあり，その部位では拡散強調画像でも高信号を示すため後部白質脳症（Posterior Leukoencephalopathy Syndrome；PLES）[2]と呼んだり，フレア（FLAIR）法を用いた検討では，皮質病変が白質病変に先行している場合もあることより，後頭→頭頂脳症（occipital-parietal encephalopathy）と命名することを唱えているグループもある．また，子癇，子癇前症は，血管内皮細胞障害のマーカー異常とは関連があるが高血圧の重症度とは関連がなく[9]，単なる妊娠時の高血圧性脳症ではないことを主張する報告[10]もみられ，この概念により各疾患特有の病態が軽視されることがないように注意が必要であろう．

3．症例呈示

以下に症例を呈示する．

48 歳，女性．子宮筋腫およびこれによる鉄欠乏性貧血により近医へ入院した．鉄剤を静注し，貧血は入院時ヘモグロビン 4.6 g/dl から 3 週間後 15.6 g/dl まで急激に改善したが，同時に血圧が 100/60 mmHg から 180/100 mmHg まで上昇していた．単純子宮全摘術を施行し術後も 200/98 mmHg と高血圧が続いていた．手術 10 時間後，数分持続する痙攣が 3 回出現し，その後，意識障害が半日続いた．さらに，16 時間後後頭部痛を訴え 21 時間後に「目がかすんで人の顔が見えない」と訴えはじめた．25 時間後に検査した MRI，第 3 病日の MRA，脳血

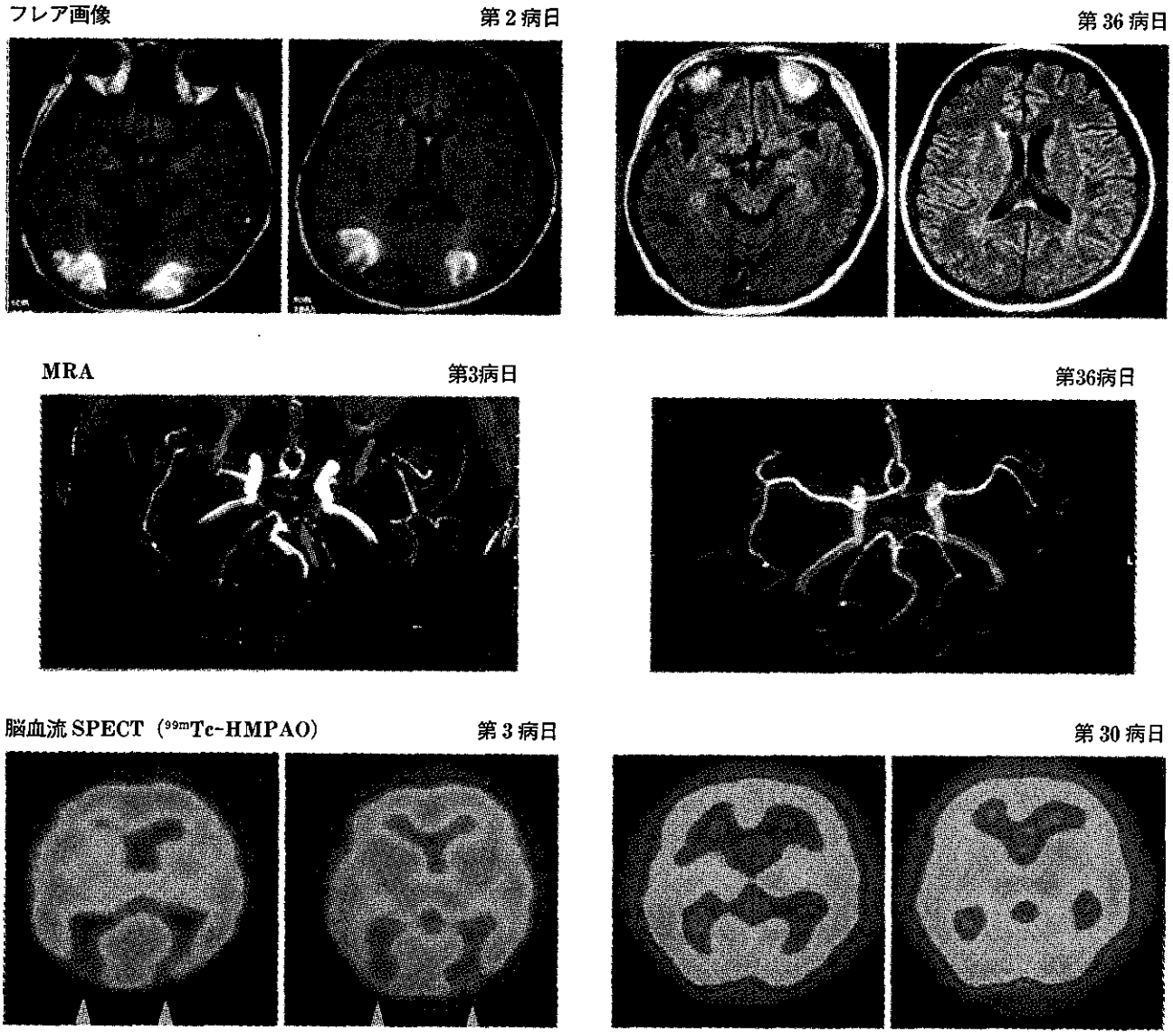

図 2. フレア画像（上段），MRA（中段），脳血流 SPECT（下段，^{99m}Tc-HMPAO）の経時変化
両側後頭葉白質に認めた高信号域および中大脳動脈，後大脳動脈の攣縮は，第 36 病日には消失している．また，両側後頭葉の血流低下も第 30 病日には改善している．

流 SPECT 検査結果を**図 2** に示す．当初，MRA 画像検査結果から血管炎による脳梗塞を疑われ，一時的にステロイドが投与され降圧薬は投与されなかった．しかし，第 4 病日には症状はほぼ消失し第 36 病日には画像上の異常所見もすべて消失した．

本症例では，急激な血圧上昇を背景にして全身麻酔時の何らかの影響が直接の引き金となり発症したと考えられた．発症までの経過は高血圧性脳症と考えられるが，降圧薬を使用せず軽快している点については高血圧性脳症とは考えにくく，このような症例は RPLS と診断すべきかもしれない．くり返し記すが，高血圧性脳症では原則としてただちに降圧を開始する必要があることはいうまでもない．しかし，複数の原因が重なっている病態では降圧せずとも症状が改善する症例もあり，本症例のように局所脳血流が低下している場合には過度の降圧が危険な場合もありうると思われる．

また，**表 1** に示したように，みかけの拡散係数測定や拡散強調画像以外の検査では，病期，重症度などにより検査所見が異なることも考えられ，脳主幹動脈病変を合併している症例ではそれが攣縮であるとは確診できない

こともありうるため，十分な病歴聴取も大切であることを改めて強調しておきたい．

4．高血圧性脳症，RPLSの降圧治療

降圧薬：推奨されている非経口降圧薬は，ニトロプルシドNa，ラベタロール，ニカルジピン，ヒドララジンなどである[8]．クロニジンは中枢神経抑制薬であるので使用すべきでない．子癇の降圧治療には，長いあいだ経験的に，ラベタロール，ヒドララジンが使用されてきた．ただし，ヒドララジンは，反射性頻脈を起こすことがあるためβ遮断薬併用を必要とする場合がある．

降圧速度および降圧レベル：Vaughanら[8]が示す方針では，降圧開始前の血圧値がいかに高くとも，治療開始1時間以内に，平均血圧を20%下げる，あるいは拡張期血圧を100 mmHg以下にする．ただし，元来，高血圧症を合併している高齢者では，逆に過度の降圧により神経症状が悪化し脳梗塞を引き起こすこともあるため注意が必要である．また，米国合同委員会第6次報告（1997年）[18]では，初期治療は数分～2時間以内の範囲で平均血圧を25%未満の範囲で下げ，次いで，脳など高血圧の標的臓器に虚血を引き起こさないように急激な降圧を避けながら，2～6時間以内に160/100 mmHgまで降圧することを推奨している．この際，一般的には即効型ニフェジピンの舌下投与が用いられることも多いが，その使用にあたり重篤な副作用も報告されており，また降圧速度や降圧レベルをコントロールできないことから，この薬剤を使用しないように警告している．

RPLSの治療：血圧上昇を認める場合には降圧治療をおこなう．ただし，免疫抑制薬が主原因の場合には同薬を減量，中止することで症状が改善することが報告されており，子癇発作ではMgの投与が効果があることが多くの研究で証明されているので，降圧レベル，降圧速度には注意し医原性に脳虚血を誘発しないようにする配慮も必要であろう．

おわりに

近年の画像診断の進歩により得られた所見から判断すると，高血圧性脳症，RPLSは，まず血管原性浮腫が起こり，重症例では微小循環不全，神経毒性浮腫も合併すると思われる．血圧上昇を認める症例では降圧を速やかに開始することが重要であることはいうまでもないが，重症例では慎重に降圧すべきであろう．

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Risk Factors Indicating Recurrent Myocardial Infarction After Recovery From Acute Myocardial Infarction

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Little is known of the risk factors of recurrent myocardial infarction (MI) among Japanese patients who have survived their first MI. The risk factors for the second MI were studied in 808 of 1,042 consecutive patients who recovered from an acute MI in Iwakuni National Hospital. Multivariate logistic regression analysis revealed that only 3 of 21 variables measured were closely related with the recurrence of MI during a follow-up period of 3.2± 4.3 years: (1) transient atrial fibrillation (relative risk (RR) 3.16), (2) previous cerebrovascular accident (RR 3.05), and (3) dyslipidemia (RR 2.19). Of the parameters of dyslipidemia, a low ratio of high-density lipoprotein-holesterol (HDL-C) to low-density lipoprotein-cholesterol (LDL-C) alone indicated subsequent MI. None of age, gender, location of the infarction, hypertension, diabetes mellitus, pulmonary congestion (Killip's class ≥2), peak serum creatine kinase activity, serum total-cholesterol, HDL- and LDL-cholesterol levels, nor smoking habit on admission was a statistically significant predictor for the second MI. The result suggests that more intensive treatment is needed for patients with the 3 risk factors. (*Circ J* 2002; **66:** 877–880)

Key Words: Myocardial infarction; Risk factors; Secondary prevention

Myocardial infarction (MI) is now one of the most frequent causes of death in elderly subjects in Japan; in 1999 approximately 15,000 cardiac deaths occurred in Japan and the majority was related to myocardial infarction (MI)[1]. Furthermore, among survivors of an acute MI (AMI), the incidence of a subsequent MI is increased 3- to 6-fold, and the risk of any cardiovascular event is as high as 80%[2]. Because patients with a previous history of cardiovascular events are at high risk for a future MI[3], aggressive management, including risk factor modification, is mandatory in this patient group[4–6]. Considerable evidence indicates that a secondary prevention program to reduce cardiovascular risk factors can favorably affect cardiovascular mortality and morbidity[7,8]. Although there are many available studies from North America and Europe regarding the risk factors for recurrent MI after the recovery from AMI[9–11], little is known concerning the Japanese population[12]. Racial differences, including genetic factors, life style, and the environmental circumstances of the patients, will affect the factors that accelerate coronary atherosclerosis and advance to subsequent MI, so we evaluated the risk factors of a recurrent MI in Japanese patients after recovery from the first AMI.

Methods

Study Patients

The study group consisted of patients experiencing their first episode of AMI who were admitted to Iwakuni National Hospital from January 1, 1991 to December 31, 2000 within 48 h of developing chest pain and who were discharged after recovery.

The diagnosis of AMI was established by the presence of 2 of the following 3 criteria: (1) elevation of serum creatine kinase (CK) more than triple the upper normal limit, (2) characteristic chest pain, or (3) ECG findings of ST-T change with evolution of the Q wave. Non-Q wave infarction was diagnosed by typical ST segment and/or T wave changes associated with serum CK elevation.

All patients were in New York Heart Association functional class I or II at discharge. The patients were followed up at the hospital or by mail at 6 and 12 months, and 5 and 10 years after discharge, and follow-up data was available from more than 90% of patients at 1 year post discharge. Patients who died from an unknown cause were excluded. Because most of the patients who had a second MI were admitted to Iwakuni National Hospital, there was no apparent difficulty in obtaining information regarding the second cardiac event.

Risk factors identified from the medical history, physical findings, laboratory data, ECG and chest X-ray were reviewed. The standard 12-lead ECG was recorded on admission, 3 h later and then once a day for 4 days. The ECG in leads CM5 and NASA was continuously monitored for at least 48 h after admission. The location of the infarction was divided into 2 groups based on involvement of the left ventricular anterior wall: (1) anterior and (2) other. Serum low-density lipoprotein-cholesterol (LDL-C) concentration was calculated from the values of total cholesterol (TC) and high-density lipoprotein-holesterol (HDL-C) and triglyceride, according to Friedewald's formula[13]. The laboratory data on admission, except for C-reactive protein (CRP), were used for analysis. The CRP concentration at discharge, instead of at admission, was used because the admission value was abnormally elevated as a result of the inflammatory nature of AMI.

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Table 1 Baseline Characteristics of the Subjects

	Re-infarction (+) (n=54)	Re-infarction (−) (n=754)	p value
Age (years)	65±10	65±12	0.82
Gender (male)	39	541	0.89
Atrial fibrillation	16	109	0.26
Transient	7	43	0.032
Chronic	9	66	0.81
Bundle branch block	7	87	0.75
Infarct site (anterior)	26	322	0.44
Heart failure (Killip2 ≥)	23	480	<0.001
Time O-A (<6 h)	39	518	0.59
Current smoking	31	393	0.45
Hypertension	24	312	0.042
Diabetes mellitus	9	165	0.37
Previous CVA	9	65	0.049
Reperfusion	21	363	0.19
PTCR	8	128	0.68
PTCA	10	132	0.85
Stenting	3	103	0.088
Dyslipidemia	34	339	0.010
Total cholesterol	207±36	193±39	0.011
LDL-C	140±32	127±36	0.017
HDL-C	44±11	45±12	0.48
HDL-C/LDL-C	0.21±0.06	0.26±0.13	0.006
Triglyceride	119±51	105±58	0.095
Uric acid	5.5±1.5	5.2±1.8	0.28
CRP	0.644±0.780	0.466±0.706	0.075
Peak CK	785±1,000	1,419±1,677	0.006

Time O-A (<6hrs), time less than 6 h from the onset to admission; CVA, cerebrovascular accident; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; CRP, C-reactive protein; CK, creatine kinase.

Data Analysis

SAS software (SAS Institute Inc Cary, NC, USA) was used for data analysis. Student's t-test was used to compare the mean values in the elderly group for continuous variables, and the chi-square test with Yates' correction was used to compare the incidence of discrete variables between groups. Standard deviations are used for continuous variables. Multivariate logistic regression analysis with a forward stepwise algorithm was undertaken to evaluate the independent importance of the variables for repeat MI. Parameter estimation was done by the likelihood ratio method, and probabilities for removal and entry of factors were set at 0.10 and 0.05, respectively. The prevalence of re-infarction in the group with a risk factor was computed and compared with that without the risk factor.

Results

Of the 1,042 patients who were admitted with their first AMI, 233 were excluded for the following reasons: 55 because of in-hospital death, 108 because of unknown cause of death after discharge, and 71 because contact with the patient was lost. Therefore, 808 patients were recruited for analysis.

During follow-up of 3.2±4.3 years, MI recurred in 54 patients (re-MI group), and 754 patients remained free from a second attack of ischemia (non-reMI group). Table 1 shows the clinical characteristics of the subjects. Hypertension was considered to be present if there was an apparent history of high blood pressure regardless of medication, or if physical examination showed elevated systolic and/or diastolic blood pressure (persistently ≥140/90 mmHg). Dyslipidemia was diagnosed when any of the laboratory-documented serum lipid concentrations on admission met the following criteria: TC ≥220 mg/dl, LDL-C ≥140 mg/dl, triglyceride ≥150 mg/dl, or HDL-C ≤35 mg/dl.

Table 2 Relative Risk (RR) of the Variables

	Relative Risk	95%CI	p value
Transient atrial fibrillation	3.16	1.24–8.02	0.016
Bundle branch block	1.27	0.54–3.01	0.588
Heart failure (Killip2 ≥)	1.34	0.73–2.46	0.348
Reperfusion	0.83	0.44–1.57	0.564
Hypertension	1.55	0.87–2.77	0.138
Previous CVA	3.05	1.38–6.74	0.006
Dyslipidemia	2.19	1.20–4.01	0.011
Total cholesterol	1.05	1.00–1.10	0.070
LDL-C	0.95	0.89–1.01	0.084
HDL-C/LDL-C	0.039	0.004–0.59	<0.001
Triglyceride	0.99	0.98–1.00	0.110
CRP	1.23	0.87–1.75	0.240
Peak CK	0.99	0.99–1.00	0.207

95%CI, 95% confidence interval; other abbreviation for Table1.

Age and gender distribution were not significantly different between the 2 groups. A similar ratio of the patients in the 2 groups arrived at hospital within 6 h of the beginning of chest pain. Successful coronary reperfusion (TIMI grade ≥2) was achieved by percutaneous transluminal coronary recanarization (PTCR), percutaneous transluminal coronary angioplasty (PTCA) or coronary stenting in 39% of the re-MI patients, and in 48% of the non-reMI group. The frequency was not different between 2 groups (p=0.19). PTCR, PTCA and coronary stenting were all carried out in similar frequencies between the 2 groups. Transient atrial fibrillation (AF) appeared within 48 h of admission in 7 patients (13.0%) of the re-MI group and 43 (5.7%) of the non-reMI group, a significantly higher incidence in the re-IM group. No significantly different incidence in chronic AF, defined as AF on admission and maintained throughout the hospitalization, was observed between the re-MI and non-reMI groups (11.1% vs 12.2%, p=0.81). Pulmonary congestion (Killip's criteria ≥2) appeared more frequently in the re-MI group (42.3%) than in the non-reMI (36.3%), and the maximum serum CK activity was lower in the re-MI group. The incidence of both hypertension and dyslipidemia was significantly higher in the reMI than in the non-reMI group. Approximately 72% and 64% of the patients, respectively, received angiotensin-converting enzyme inhibitor (ACEI) and/or aspirin at discharge, and the rates of each medication were not different between the 2 patient groups.

The results of multivariate logistic regression analysis are shown in Table 2. Variables with an arbitrarily defined p<0.1 in univariate analysis were selected for entry into the model, and 9 of 21 variables met this criterion. Of these 9, only 3 were independent factors related to a subsequent attack of MI: (1) transient AF, (2) dyslipidemia and (3) previous cerebrovascular accident. The relative risks (RR) of these 3 variables calculated in the presence of other covariables were 3.16 (95% confidence interval (CI), 1.24–8.02, p=0.016), 2.19 (95%CI 1.20–4.01, p=0.011), and 3.05 (95%CI 1.38–6.74, p=0.006), respectively. Furthermore, we calculated the RR using the variables of TC, LDL-C, the ratio of HDL-C/LDL-C and triglyceride instead of dyslipidemia with other covariables. Because univariate analysis did not provide a difference in the HDL-C concentration of p<0.1 between the 2 groups, the

serum HDL-C concentration was not included in the calculation. Of the measurements of serum lipid concentration, only the ratio of HDL-C/LDL-C, in addition to transient AF and previous cerebrovascular accidents, was related to a second ischemic attack; TC and LDL-C tended to be related to a subsequent MI, but the association did not reach a statistically significant level.

Discussion

It is fortunate for this study that almost all AMI patients in Iwakuni City and nearby towns are brought to Iwakuni National Hospital, which is the only hospital in this area for sophisticated treatment of cardiac infarction. Furthermore, more than 2-thirds of the patients attended the ambulatory clinic on a regular basis, which made follow up simple and easy.

In the present study of 808 patients, transient AF, dyslipidemia and previous cerebrovascular accident were related with an average increase of 3.16, 2.19 and 3.05 times, respectively, to the risk of subsequent MI. Although in our univariate comparison of 21 factors, 9 obtained entry into the multivariate logistic regression model using dyslipidemia, only 3 remained statistically significant by the forward stepwise method for predicting a recurrent ischemic attack.

Although many risk factors have been proposed for AMI, the established major ones are obesity, hyperlipidemia, hypertension, cigarette smoking and diabetes mellitus;[14,15] and epidemiological studies have clearly demonstrated synergy of these risk factors![16,17] The present study confirmed that hyperlipidemia, especially a low HDL-C/LDL-C, was a significant causative factor of re-infarction after recovery from the first MI. TC and LDL-C concentrations tended to be related with the recurrence of MI but did not reach a significant level. The Miyake and Fukuoka Heart Study group proved that hypercholesterolemia was an important risk factor for the first MI in patients aged 40–64 years, but not in the elderly group over 64 years of age![18] The mean age of the present subjects was 65 years and the age distribution may be the reason why the TC and LDL-C concentrations did not show a significant relationship with the recurrence of MI. Serum triglyceride and HDL-C concentrations did not correlate with re-infarction in this study. Although some investigations have shown that the serum TC has a predictive value for re-infarction in elderly persons with coronary heart disease;[19] others have observed that serum cholesterol levels determined after MI did not have prognostic value![20,21] Finding that the cholesterol measurements done during the acute phase after infarction have predictive value creates a problem, because cholesterol concentrations may actually fall spontaneously during this period![22] Although we used data obtained within 48 h of the onset of MI to avoid the effect of the spontaneous decrease in cholesterol during the acute phase, the rapid fall in cholesterol concentration during this period may still have affected the results. Schlant et al[23] observed a significant inverse relationship of triglyceride concentrations to the 5-year event rate in survivors of MI, and a positive relationship between the serum triglyceride concentration and the 3-year cardiovascular mortality rate was reported by Frost et al![24] No relationship of the serum triglyceride concentration to the incidence of re-infarction could be made in the present study because on average the serum triglyceride concentration was almost within the normal range, even in the re-infarction group. Although hypertension, cigarette smoking and diabetes mellitus are well-known major factors, as shown in many epidemiological studies, our investigation failed to provide a role for these variables in the recurrence of AMI. A possible explanation is that both conditions were well controlled by diet and, when necessary, medications, and all the patients had stopped smoking after the first AMI. Another explanation is that different factors from those of the first MI are involved in the progression of the second MI in patients with preceding severe coronary sclerosis. Because we did not analyze the follow up data of blood pressure and blood glucose concentrations in the patients, we cannot explain the reason(s) for the lack of a relationship between these variables and re-infarction.

It should be noted that transient AF early after the infarction was a significant indicator of subsequent MI, although this arrhythmia was observed only in 50 (6.2%) of the studied patients. Few investigations have studied the relationship between recurrent MI and transient AF just after the first attack. Suarez et al observed no significant relation between mortality and previous AF![25] but Petretta et al[26] compared the prognoses of 163 patients aged 40–69 years, with 112 patients older than 70 years, and showed a poorer 1-year prognosis and greater prevalence of AF in the elderly patients than the younger group. In the study by the Coronary Drug Project Research Group[23] in which the natural history of 2,789 patients who had recovered from MI was investigated, 40 variables were analyzed, but not AF. The prevalence of transient AF is somewhat underestimated in the present study. Because the ECG was continuously monitored in all patients with AMI for at least 4 days after admission, few cases would have escaped documentation of arrhythmias during their stay in the hospital; however, we could not estimate how many patients developed transient AF in the pre-hospital phase just after the onset of the attack.

Study Limitations

In this study, 108 patients were excluded from analysis because of an unknown cause of death and this number was almost double that of patients with apparent re-infarction. We suppose that because some of those 108 patients died from a second MI, that patient data would influence the results of this study.

The patients were recruited for 10 years from 1991 to 2000 and during this interval, methods of treatment for coronary heart disease, including coronary interventions and medications for hyperlipidemia and hypertension, changed dramatically. Although we observed a similar frequency of coronary interventions between re-MI and non-reMI groups, no data of the medications used during the follow up period were available and the treatment in this period would affect the prognosis of the patients.

In conclusion, transient AF, a history of a cerebrovascular accident and a low serum HDL-C/LDL-C ratio in patients who survived an AMI were important predictors of a recurrence of MI. The result suggests that more intensive treatment is needed to prevent a second episode of MI in the patients with these risk factors.

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Report

Japanese Society of Hypertension (JSH) Guidelines for Self-Monitoring of Blood Pressure at Home

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Home blood pressure (BP) measurements are indispensable for the improvement of hypertension management in medical practice as well as for the recognition of hypertension in the population. The Working Group for Establishment of Guidelines for Measurement Procedures of Self-Monitoring of Blood Pressure at Home of the Japanese Society of Hypertension has established standards for all techniques and procedures of home BP measurements. The recommendations are as follows. Recommendation: 1) Arm-cuff devices based on the cuff-oscillometric method that have been validated officially, and the accuracy of which has been confirmed in each individual, should be used for home BP measurement. 2) The BP should be measured at the upper arm. Finger-cuff devices and wrist-cuff devices should not be used for home BP measurements. 3) Devices for home BP measurement should be adapted to the American Association for Medical Instrumentation (AAMI) standards and the British Hypertension Society (BHS) guidelines. In addition, the difference between the BP measured by the auscultatory method and that measured using the device should be within 5 mmHg in each individual. The home measurement device should be validated before use, and at regular intervals during use. 4) Home BP should be monitored under the following conditions. The morning measurement should be made within 1 h after waking, after micturition, sitting after 1 to 2 min of rest, before drug ingestion, and before breakfast. The evening measurement should be made just before going to bed, sitting after 1 to 2 min of rest. 5) Home BP should be measured at least once in the morning and once in the evening. 6) All home BP measurements should be documented without selection, together with the date, time, and pulse rate. Use of devices with a printer or an integrated circuit memory is useful to avoid selection bias. 7) The home BP in the morning and that in the evening should be averaged separately for a certain period. The first measurement on each occasion should be used for totaling. 8) Home BP values averaged for a certain period indicate hypertension when 135/80 mmHg and over and definite hypertension when 135/85 mmHg and over. Normotension is defined as less than 125/80 mmHg and definite normotension as less than 125/75 mmHg. Home BP measurements based on these guidelines can be considered an appropriate tool for clinical decision-making, and it is hoped that these guidelines will serve to reduce confusion and confirm the place of home BP measurement in clinical practice. (*Hypertens Res* 2003; 26: 771–782)

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