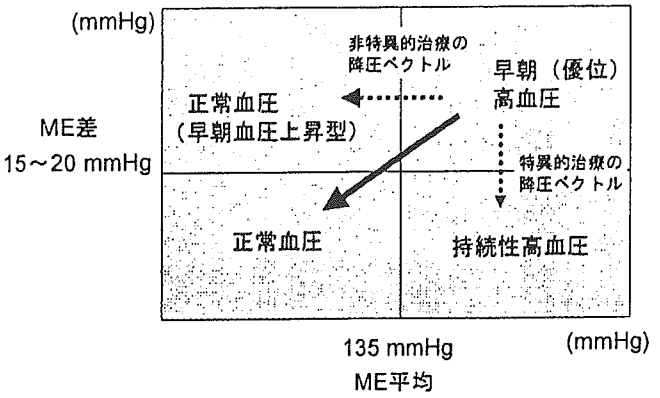

図57　家庭血圧を用いた早朝高血圧に対する降圧療法
（自治医科大学）
非特異的治療：長時間作用型降圧薬（朝夕の2分割処方も考慮），利尿薬
特異的治療：α遮断薬の就寝前投与
レニン-アンジオテンシン-アルドステロン系抑制薬（就寝前投与も考慮）
心拍数を抑制するCa拮抗薬（シルニジピン，アゼルニジピン，ジルチアゼム）

Ca拮抗薬も特異的治療の特徴を有する。

次に，診察室血圧と家庭血圧が正常レベルでも，睡眠時無呼吸症候群が疑われたり，臓器障害や糖尿病などを合併している夜間血圧変動異常のハイリスク群（表4）では，ABPMを用いて夜間血圧を測定することが望ましい。最近では，夜間血圧を測定できる家庭血圧計も開発されつつある。この夜間血圧のコントロールに対しても，薬剤間で効果が異なる。利尿薬ではnon-dipperをdipperに変える効果が認められることから，夜間高血圧患者にはよい適応になる[107]。しかし，利尿薬は夜間の最低血圧，たとえば収縮期血圧が100 mmHgでも，さらに低下させる。長時間作用型Ca拮抗薬の夜間睡眠時血圧と昼間覚醒時血圧の降圧割合は同程度である[91,189]。したがって，dipperでの高い昼間覚醒時血圧の降圧程度は，低い夜間睡眠時血圧の降圧程度より大きい。すなわち，夜間血圧を変化させることなくdipperのまま降圧する。non-dipperでは，昼夜同程度に下降し，non-dipperのまま下降することが多い。extreme-dipperに対しては，おもに昼間の高血圧レベルが下降し，dipperになる傾向にある[91]。ACE阻害薬やAII受容体拮抗薬等のR-A系抑制薬は，降圧効果が24時間持続しないものも多いが，長時間作用型もしくは朝夕2分割処方をした場合，non-dipperをdipperに変える可能性がある。ACE阻害薬やAII受容体拮抗薬は利尿薬を併用しない単剤治療の場合，夜間ならびに早朝高血圧の抑制効果は長時間作用型Ca拮抗薬アムロジピンより弱い[189,190]。しかし，同じAII受容体拮抗薬のなかでも，降圧効果がかなり異なり，早朝高血圧の抑制作用が強いものもある[191]。また，ACE阻害薬の就寝前服用は，早朝の起床前の血圧レベルを有意に低下させることから[192]，早朝血圧コントロール不良例ではR-A系抑制薬の就寝前投与も考慮される。R-A系抑制薬は降圧効果に加え，血管壁R-A系を抑制することにより大血管stiffnessと圧受容体反射を改善し，血圧変動性を減少させることが期待されているが，現在，まだ十分なエビデンスはそろっていない。α遮断薬は血圧日内変動異常を是正する傾向にある[101,170～172]。すなわち，extreme-dipperとnon-dipperはdipperに改善し，血圧モーニングサージを選択的に抑制する。

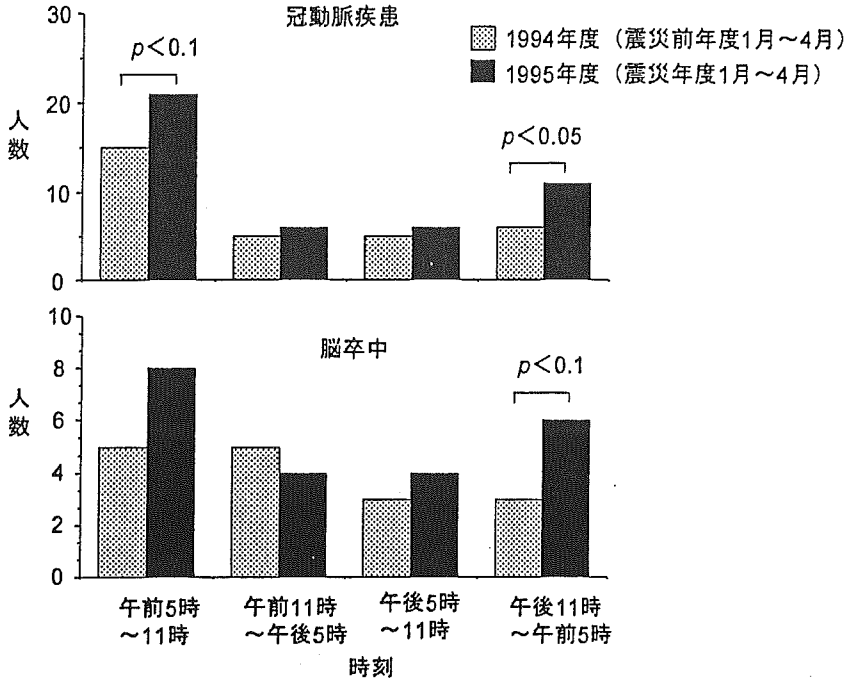

図58　阪神淡路大震災時（1995年1月17日発生）の震源地における心血管イベント死亡と発症時刻（文献200，201）

6. ストレスと心血管リスク

近年，精神心理ストレスが新規の心血管リスクとして注目を集めている[109,193～195]。著者は1995年度の阪神淡路大震災時には，その震源地に位置する北淡町国民健康保険北淡診療所に勤務していた。その際の継続した地域診療を通じて，強度のストレスの心血管リスクへのインパクトを評価することができた[194,196～198]。

兵庫県津名郡医師会で震災後の心血管死亡を調査した[199～201]。前年度の1994年と比較した震災後1995年度の心血管死亡の発症時間帯別の頻度を示す（図58）。震災前年をみると，冠動脈疾患，脳卒中ともに他の時間帯に比較し，早朝から午前中にかけての時間帯に好発していることが伺える。震災後さらにその時間帯の心血管死亡が増加している。最も明らかな震災後の心血管死亡の増加は，普段は就寝している夜間から早朝にかけての時間帯にみられた。しかし，昼から夜就寝するまでの活動時間帯の増加はまったくなかった。以上のように，強烈なストレス下では心血管イベント発症の好発時間帯が変化することが明らかになった。これまでにも，ロサンゼルスのノースリッジ地震やイラクのミサイル攻撃などのストレスにより，その被害地域の心血管イベントが増加することが報告されている[202,203]。

震災ストレス時には血圧は1～2週間にわたり一過性に上昇するが，通常4週間目には低下する[204～206]。しかし，微量アルブミン尿症を伴う高血圧患者では震災後の血圧上昇が遷延した（図59）。同じ検討を，心電図の左室肥大ならびに無症候性脳梗塞でも行ったが，震災後の血圧上昇の遷延には関連がみられなかった。したがって，微量アルブミン尿は他の高血圧性臓器障害のなかでもストレス時の高血圧の成立に重要な役割をもつと考えられる。

また，白衣高血圧の患者においては，震災後に24時間血圧レベルも上昇していた[49]。このことは，ストレスが加わった場合，白衣高血圧が持続性高血圧に移行することがあることを示している。同様の移行は震災ストレスのみならず，家庭内ストレスなどによっても生じる[50]。しかし，ス

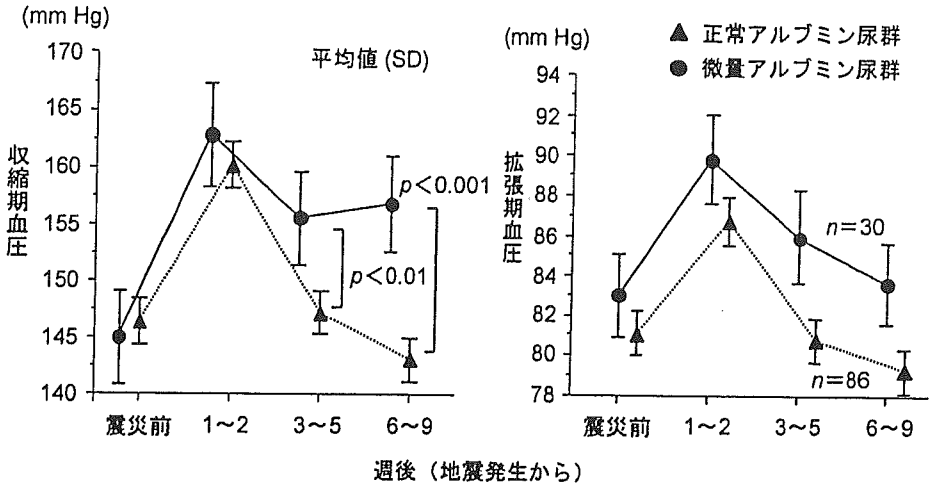

図59　震災時の高血圧患者の血圧上昇と微量アルブミン尿症（文献49, 206）

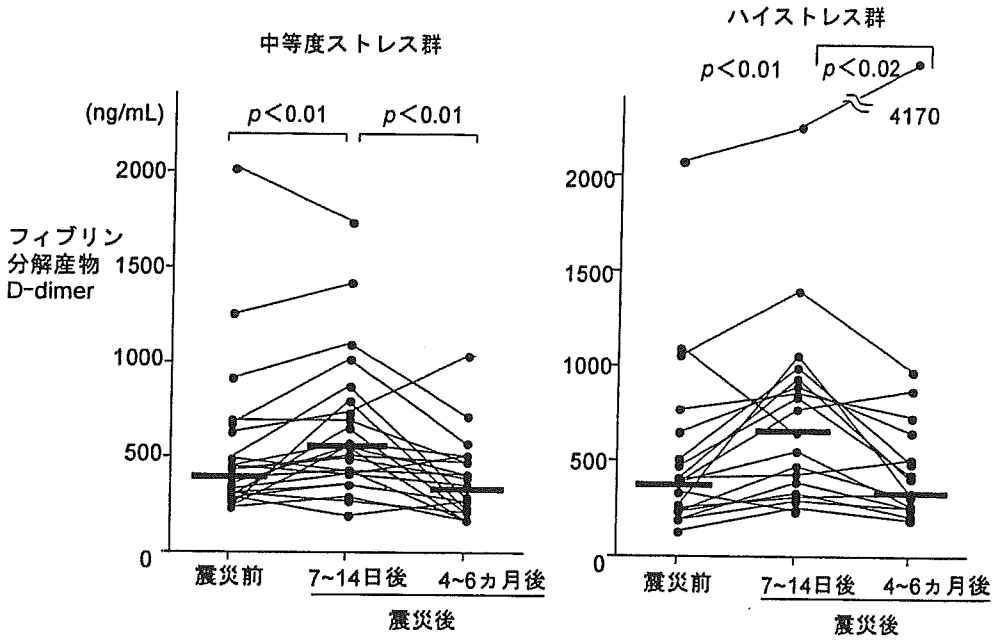

図60　震災時のストレスと血栓マーカー（文献208）

トレスが去った後には再び白衣高血圧に戻ることから，白衣高血圧は経時的に保持される[51]。これらのストレス時の特徴を知り，災害時の血圧管理を行う必要がある[207]。

阪神淡路大震災時の高血圧外来患者の経時的診療の際に，これらの血液凝固・線溶系因子を測定した。図60に震災時の高血圧外来患者の凝固・線溶系因子の変動を示す[208]。震災後の急性期1～2週間に最も著明に増加したのはD-dimerで，その上昇は震災により家族の入院もしくは家屋の全壊をきたしたハイストレス群で，それ以外の中等度ストレス群に比べ，より著明であった。この凝固・線溶系亢進状態は，心血管イベントの増加が例年と同様になった4～6カ月後には改善していた。また，フィブリノーゲンとともに血液粘度規定因子であるヘマトクリットの増加，血圧増加も認められたが，血清脂質に変動はなかった。これらの血栓性因子には日内変動がみられ，

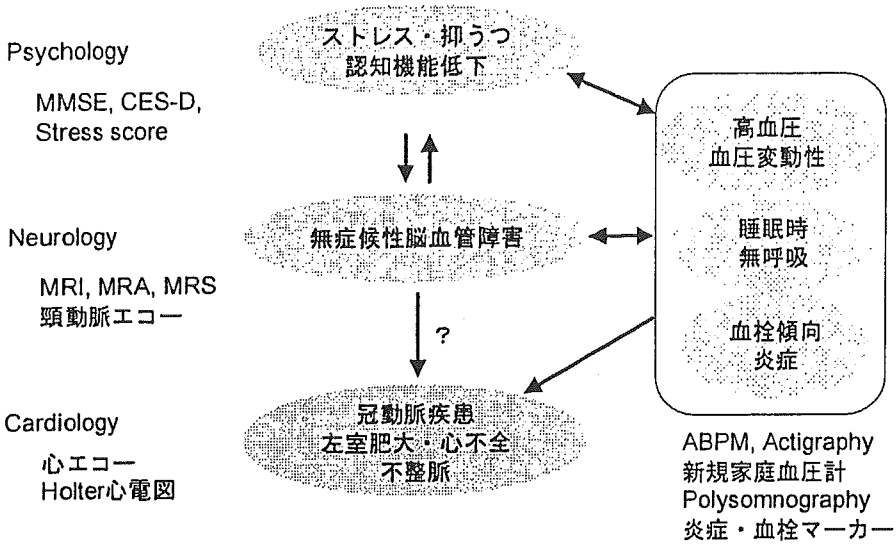

図61　自治医科大学高血圧研究－Psychoneurocardiology：Brain and The Heart

早朝に増悪することが知られている。

この震災時の夜間発症の心血管系疾患のメカニズムを考えるに，夜間に増幅される震災時の恐怖や睡眠環境の変化による睡眠障害や，それに基づく微小覚醒や夜間行動の増加が誘因となった可能性がある。これらの誘因が，通常は副交感神経優位であるはずの夜間に，交感神経活性化を引き起こし，自律神経バランスの変動およびそれに基づく脈拍や血圧変動をもたらしたものと推測される。また，夜間には心筋虚血の閾値の低下も生じる。したがって，急性危険因子の夜間改善が不十分で，夜間の発症閾値が低い血栓準備状態にある高齢者に，選択的に夜間発症の心血管イベントが発生した可能性がある。

このように，精神心理ストレスは心血管疾患を増加させ，その発症時間帯も修飾する。そのメカニズムにはおもに交感神経に関連した生体負荷で修飾される血圧変動や，血栓性リスク因子などの急性リスク因子がかかわっていると考えられる[209]。これらの要因は日内変動を有し，早朝に増悪する。ストレスや睡眠環境変化によりもたらされた睡眠障害や夜間行動の変化も急性リスク因子の日内変動リズムに影響を与え，早朝および夜間発症の心血管イベントの発症を増加させる可能性がある。

7. 今後の展望

現在の高血圧診療ガイドラインでは，心血管リスク因子や臓器障害の合併と血圧レベルに基づくリスクの層別化と治療が行われている。この2つの基軸に加えて，血圧変動性の心血管イベントのトリガーとしての重要性を，早朝，身体活動，ならびに精神心理ストレスでの状況特異的な血圧変動性をより正確に測定する生体モニタリング装置を開発することにより，証明したい。

21世紀は脳研究の時代といわれ，神経科学分野の著しい進歩とともに，脳がどのような経路で全身臓器をコーディネートしているかが，次第に解明されてきている。今後，精神心理ストレスや無症候性脳疾患が高血圧や心血管リスクの日内変動と関連して，どのように循環器疾患の発症に関与するかを明らかにするPsychoneurocardiology：Brain and The Heart（図61）という領域の研究を進め，高血圧個別診療に生かしていきたいと考えている。

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早朝高血圧のリスクマネジメント

Clinician's Manual on Early Morning Risk Management in Hypertension

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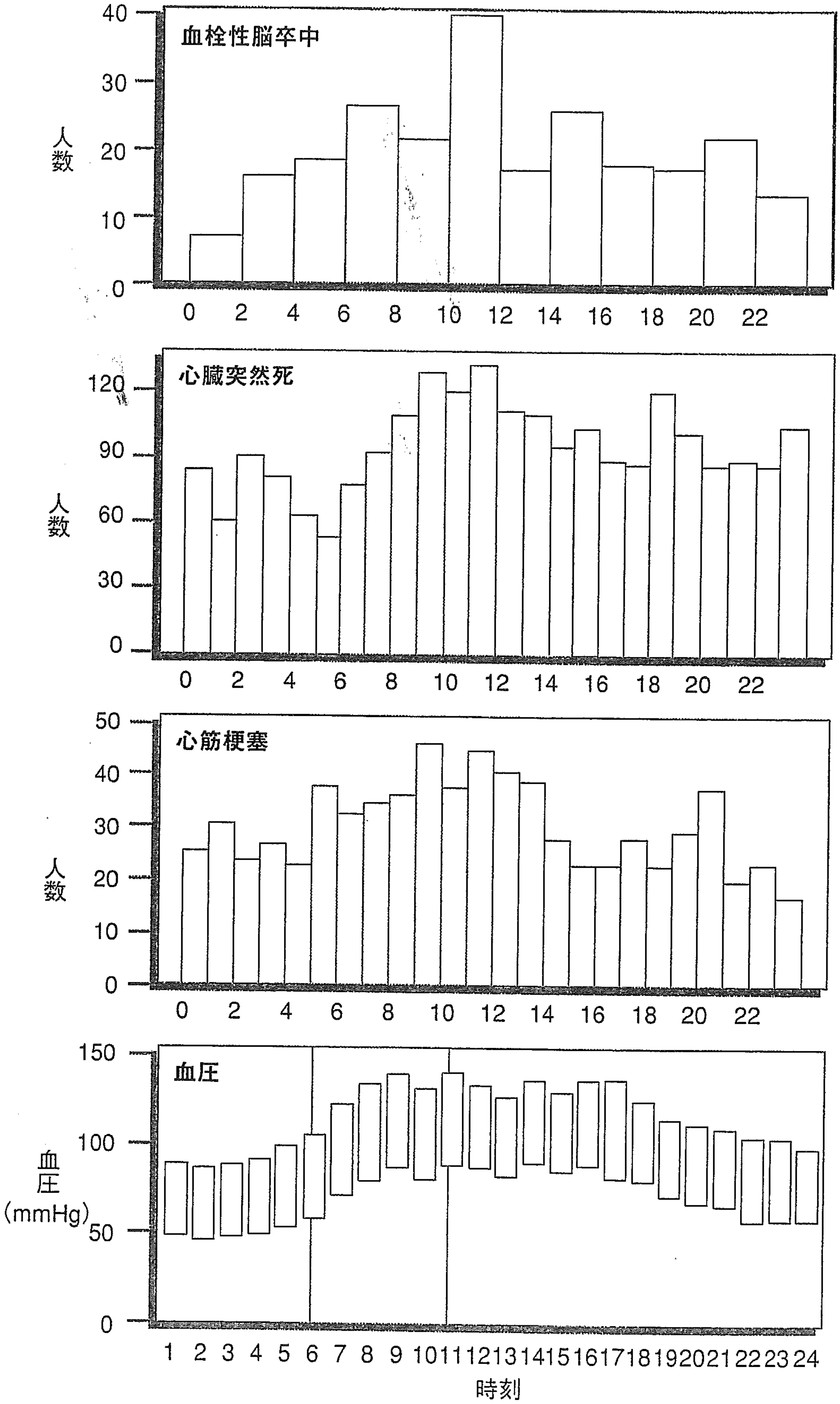
第1章

夜間の血圧下降

心筋梗塞や心臓突然死などの心血管イベントの発現には、明らかに好発時間帯が認められる。虚血性あるいは出血性の脳血管障害の発現もまた、早朝から午前中、とくに午前6時から正午の間に発現することは、よく知られている（図1-1）[1-8]。自由行動下における血圧の日内変動においても、早朝から午前中にかけて最も高値を示し、その後次第に下降し、深夜に最も低い値を示すことが知られている [7]。こうした血圧の日内変動には、臨床的に2つの重要なポイントがある。1つは深夜の血圧下降、もう1つはモーニングサージと呼ばれる早朝の血圧上昇であり、この2つの現象にはある程度の関連がある。

正常血圧の健常人においても血圧の明らかな日内変動がみられ、夜間には10～20%の下降が認められる。健常人の血圧の日内変動は、心理的あるいは身体行動などのさまざまな要因によって規定され [9,10]、また同時に、交感神経系（図1-2）[11] やレニン・アンジオテンシン・アルドステロン系（RAAS；図1-3）[12] を含む神経体液因子にも支配されている。高血圧性標的臓器障害を伴っていない高血圧患者においては、通常、正常なパターンの血圧日内変動が観察される。しかし、高血圧患者の中に血圧日内変動のパターンに異常を示す患者群が認められる。これら日内変動パターンに異常を呈する患者では、その進展の度合いに差はあるものの、高血圧性標的臓器障害を有することが多く、将来の心血管イベントの発現が予測されうるとの研究結果が報告された [13-22]。これは、24時間自由行動下における血圧の測定値レベルとは独立した事象であると考えられている。

図1-1 心血管イベントの発生時間と血圧日内変動



（*Circulation* 1989; 79: 733-743の改変）