the lifestyle related risk factors for SLE among the Japanese population,[6,11] they did not estimate the risk of SLE after controlling for other factors. As far as we know, this is the first report showing that smoking is a risk factor for SLE among Japanese females after controlling for age and other factors.

In conclusion, the present study may support the belief that smoking is a risk factor for SLE among Japanese females. In addition to smoking, walking, leisure-time physical exercise, and high frequency of drinking were proposed as the probable risk factors. On the other hand, sufficient sleep is suggested as a preventive factor. However, further studies are required to confirm the results of the present study.

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Special Report

パーキンソン病関連疾患の性差

Sex Difference in Parkinson's Disease

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Key Words
パーキンソン病（Parkinson's disease），性差（sex difference），臨床症状（clinical symptoms），Hoen-Yahrの臨床重症度分類（Hoehn and Yahr staging scale）

はじめに

パーキンソン病（パーキンソン病と進行性核上性麻痺，大脳皮質基底核変性症）は，1978年に特定疾患治療研究事業の対象疾患として医療費公費負担制度が適用され，2003年10月にパーキンソン病関連疾患に名称が変更された。2003年度のパーキンソン病関連疾患の医療受給者数は，地域保健老人保健事業報告[1]によれば，7万532人と，潰瘍性大腸炎に次いで多い。パーキンソン病関連疾患は，パーキンソニズムなどの錐体外路徴候のほか，自律神経症状，小脳症状，抑うつ，失神，構音障害など多くの臨床症状を呈する疾患であり，これまでに患者の神経症状や自律神経症状，精神症状の頻度などが報告されている。また，パーキンソン病関連疾患患者の重症度の指標として，Hoen-Yahrの臨床重症度分類（以下Yahrの臨床重症度）がわが国で一般的に使用され報告されている。

特定疾患治療研究事業対象疾患については，2003年度より，特定疾患の医療受給の申請時に提出される臨床調査個人票が電子入力されるようになったため，受給者の性，年齢，推定発病年齢，受療状況，ADL，要介護度，身体障害手帳交付の有無のほか，臨床症状，検査所見，治療方法，合併症などの情報を系統的に集計解析することが可能になった。2003年度に電子入力された臨床調査個人票は，受給者全体の50%弱であるが，性，年齢別入力状況に大きな差がないため，疾患ごとの臨床症状についての検討が可能である[2]。そこでこのデータを用いて，わが国のパーキンソン病関連疾患の受給者（男性1万2,395人，女性1万7,836人）の性別の臨床像の違いを明らかにする。解析した重症度や症状の区分は，**表1**に示すとおりである。

医療受給者の年齢と発病年齢と発病からの期間の性差

年齢別医療受給者数は，男女とも60～80歳代が多く，70歳代が全体の約45%を占めて最も多い（**図1**）。医療受給者の平均年齢は男性が70.2歳で女性が72.4歳で女性が2.2歳高い。性別発病時年齢別医療受給者数は，男女

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表1　解析項目

・Yahrの臨床重症度
1度　一側性パーキンソニズム
2度　両側性パーキンソニズム　姿勢反射障害なし
3度　軽～中等度パーキンソニズム　姿勢反射障害あり　日常生活に介助不要
4度　高度障害を示すが，歩行は介助なしにどうにか可能
5度　介助なしにはベッド車椅子生活

・日常生活機能障害度（厚生労働省研究班）
1度　日常生活，通院にほとんど介助を要しない
2度　日常生活，通院に部分的介助を要する
3度　日常生活に全面的介助を要し独力では歩行起立不能

・神経症状の重症度（7項目）
（1）静止時振戦
0．なし
1．ごくわずかでたまに出現
2．軽度の振幅で持続的に出現か，中等度の振幅で間歇的に出現
3．中等度の振幅で大部分の時間出現
4．大きな振幅の振戦が，大部分の時間出現

（2）指タップ（母指と示指をできるだけ大きな振幅でタッピング）
0．正常
1．やや遅いか，振幅がやや小さい
2．中等度の障害　早期に疲労を示す。動きが止まることもある
3．高度の障害　運動開始時からリズムが乱れ，時に動きが止まる
4．ほとんどタッピングの動作にならない

（3）筋強剛
0．なし
1．軽微な固縮，または他の部位の随意運動で誘発される固縮
2．軽度～中等度の固縮
3．高度の固縮，しかし関節可動域は正常
4．著明な固縮。正常可動域を動かすには，困難を伴う

（4）椅子からの立ち上がり
0．正常
1．可能だが遅い。一度でうまくいかないこともある
2．肘掛けに腕をついて立ち上がる必要がある
3．立ち上がろうとすると倒れこむことあり。しかし最後には独力で立ち上がれる
4．立ち上がるには介助が必要

（5）歩行
0．正常
1．緩慢，小刻み・引きずりも出現。加速歩行や突進はない
2．困難だが独歩可能。加速歩行，小刻み歩行，前方突進，すくみが出現することあり
3．すくみや高度の歩行障害があり，歩行に介助を要する
4．介助があっても歩けない

（6）姿勢
0．正常
1．軽度の前屈姿勢（高齢者では正常の範囲内）
2．中等度の前屈姿勢,一側にやや傾くこともある
3．高度の前屈姿勢，脊椎後彎を伴う。一側へ中等度に傾くことあり
4．高度の前屈，究極の異常前屈姿勢

（7）姿勢の安定性（立ち直り反射障害と後方突進現象）
0．なし
1．後方突進現象があるが，自分で立ち直れる
2．後方突進現象があり，支えないと倒れる
3．極めて不安定で，何もしなくても倒れそうになる
4．介助なしには起立が困難

・その他の臨床症状（21項目）

排尿困難	幻覚	垂直性核上性眼球運動障害
失禁	失語	持続性注視方向性眼振
陰萎	失認	進行性の構音障害
頑固な便秘	失行	体幹部や頚部に強い筋強剛
失神	肢節運動失行	小脳症状
痴呆	他人の手兆候	四肢の腱反射
抑うつ	四肢症状の非対称性	バビンスキー兆候

とも50～70歳代が多く，60歳代が約35%を占めて最も多い（図2）。発病時年齢の平均は男性が61.5歳で女性が63.1歳で女性が1.6歳高い。性別発病後期間別医療受給者数は，男女とも5年以上10年未満が約35%で最も多い。発病後期間の平均は男性が8.6年で女性が9.2年である。

医療受給者の臨床像の性差

Yahrの臨床重症度は，3度以上の者は男女とも約95%で，4度以上の者は男性は45.9%，女性は54.0%で女性のほうが重症度が高い。これを年齢別に見ると，男女とも年齢が高くなるにつれて重症度が高い者の割合が増えるが，どの年齢もおおむね女性の重症度が高い（図3）。

日常生活機能障害度は，2度以上の者は男女とも約95%で，3度以上の者は男性は25.8%，女性は33.8%で女性のほうが重症度が高い。年齢別にみると，男女とも年齢が高くなるにつれて障害度が高い者の割合が増えるが，どの年齢もおおむね女性の重症度が高い（図4）。

神経症状の重症度は，1度以上のものは，指タップ，筋強剛，立ち上がり，歩行，姿勢，姿勢安定性が男女とも90%以上で，静止時振戦が男女とも約80%である。3度以上の者は立ち上がり，歩行，姿勢，姿勢安定性で女性のほうが多く，静止時振戦，指タップ，筋強剛では3度以上の者は男女とも同程度である（図5）。年齢別に

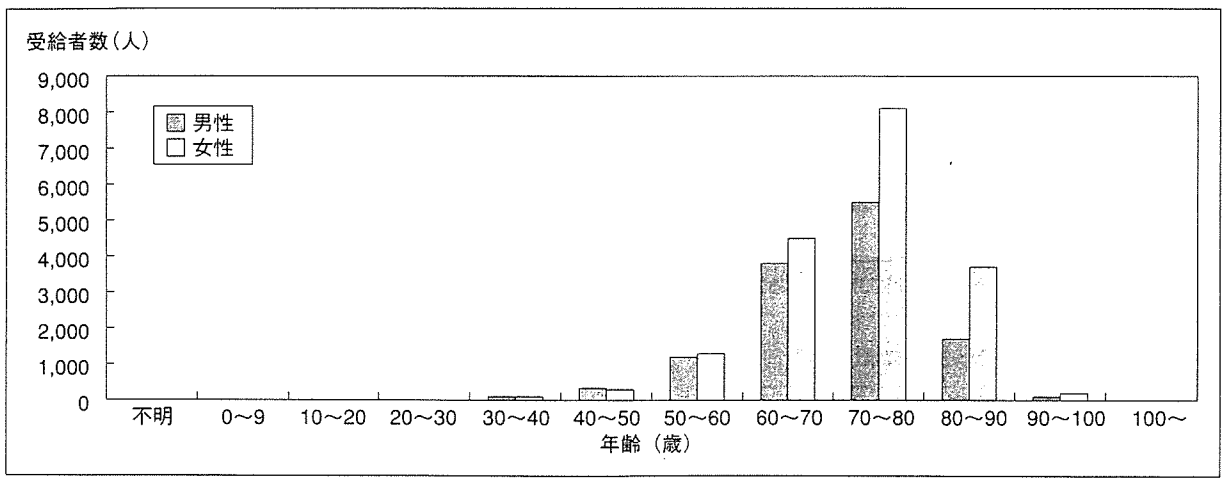

図1　性別・年齢別受給者数

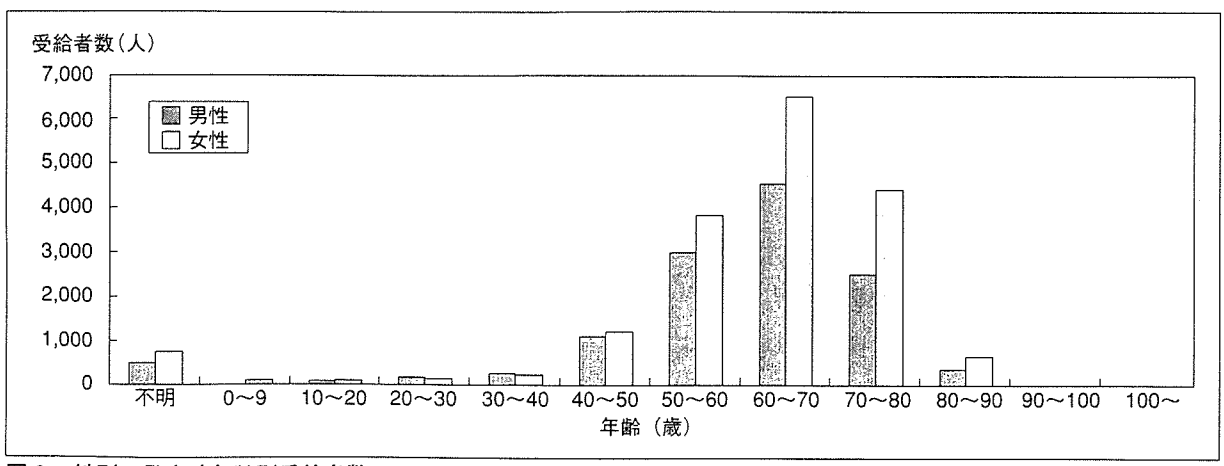

図2　性別・発病時年齢別受給者数

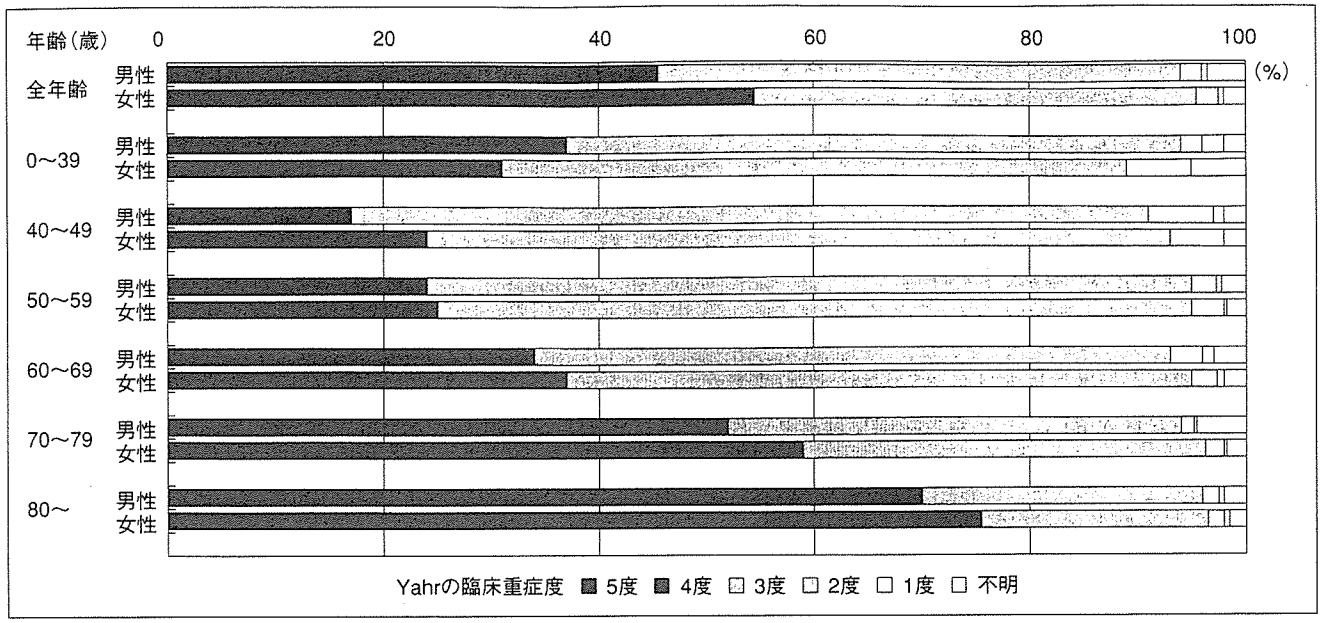

図3　性別年齢階級別Yahrの臨床重症度

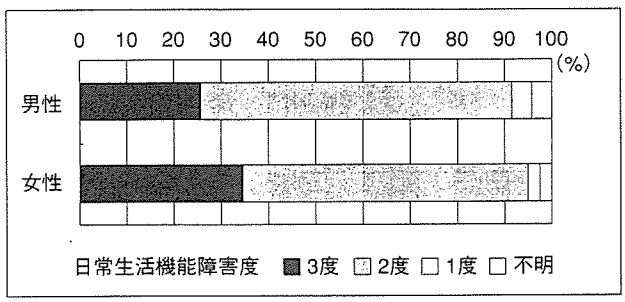

図4　性別日常生活機能障害度

みると，7項目とも年齢が高くなるにつれて男女とも重症度3以上の者の割合がおおむね高くなる。また，立ち上がり，歩行，姿勢，姿勢安定性の重症度3以上の者の割合は，どの年齢においてもおおむね女性のほうが男性よりも高い。

性別その他の臨床症状ありの者の割合は，頑固な便秘が男性で58.9%，女性で56.6%と最も高く，以下男性では，排尿困難，失禁，陰萎の順に高く，女性では抑うつ，失禁，痴呆の順で高い。排尿困難，失神，進行性の構音障害，垂直性核上性眼球運動障害は男性が女性より高く，抑うつは女性が男性より高い（図6）。年齢別にみると，排尿困難は50歳以上で男性が高く，失神と垂直性核上性眼球運動障害は60歳以上で男性が高く，抑うつ症状は50歳以上で男性が高い（図7）。

まとめ

わが国のパーキンソン病患者の平均年齢は過去の調査では，男性61.4歳，女性61.9歳[3]，と報告され，性差はみられていない。今回は男女とも過去に比べ平均年齢が10歳近く高く，女性のほうが男性に比べて高かった。ただし，特定疾患治療研究事業におけるパーキンソン病の対象範囲は，Yahrの臨床重症度が3度以上かつ日常生活機能障害度が2度以上の者と定めているため，より軽度の患者を含めた平均年齢は今回の結果より低くなると考えられる。

パーキンソン病の平均発病年齢は過去の調査では男性55.8歳，女性56.8歳と報告され，性差はみられていない[3]。今回は過去の報告と比べて男女とも平均発病時年齢は5歳近くとやや高く，女性のほうが男性に比べて高かった。

Yahrの臨床重症度の性差について報告はこれまでなかった。しかし今回の結果では，Yahrの臨床重症度と日常生活機能障害度が高いものの割合が女性で男性よりやや多いという結果が得られ，Yahrの臨床重症度の性

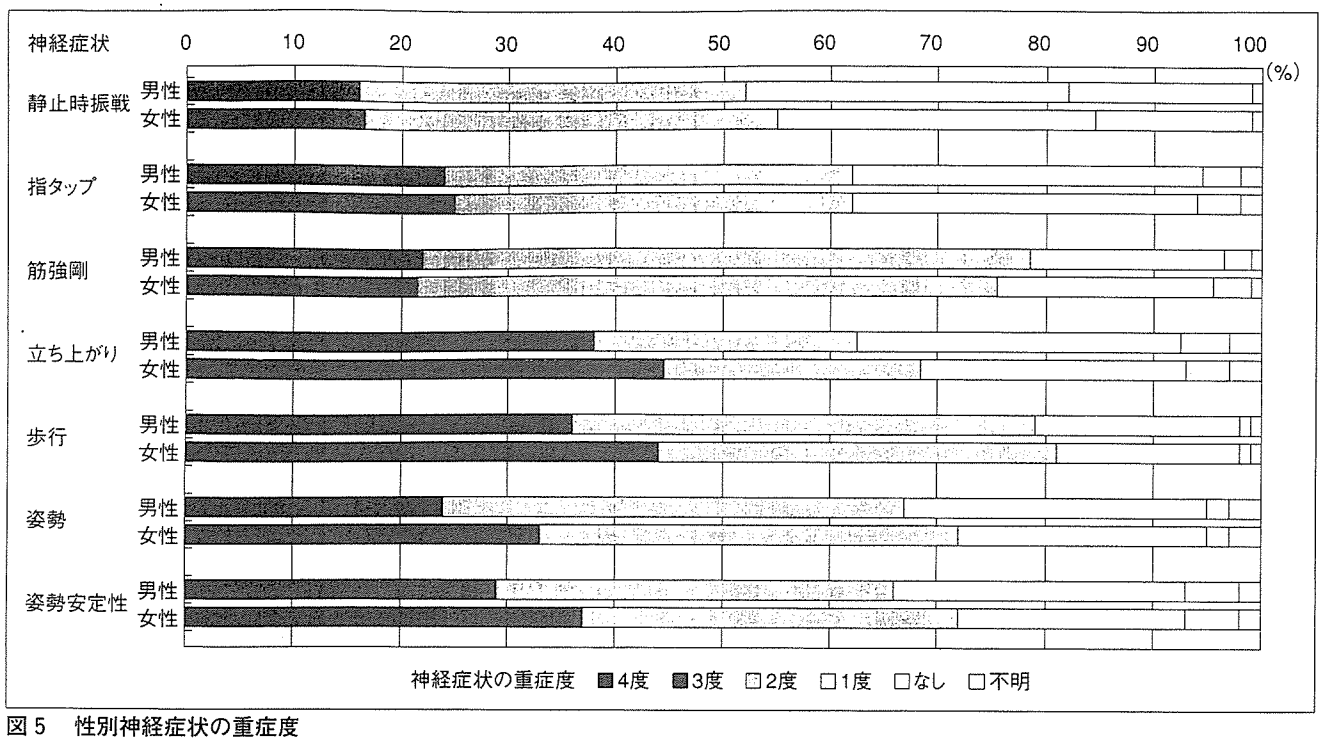

図5　性別神経症状の重症度

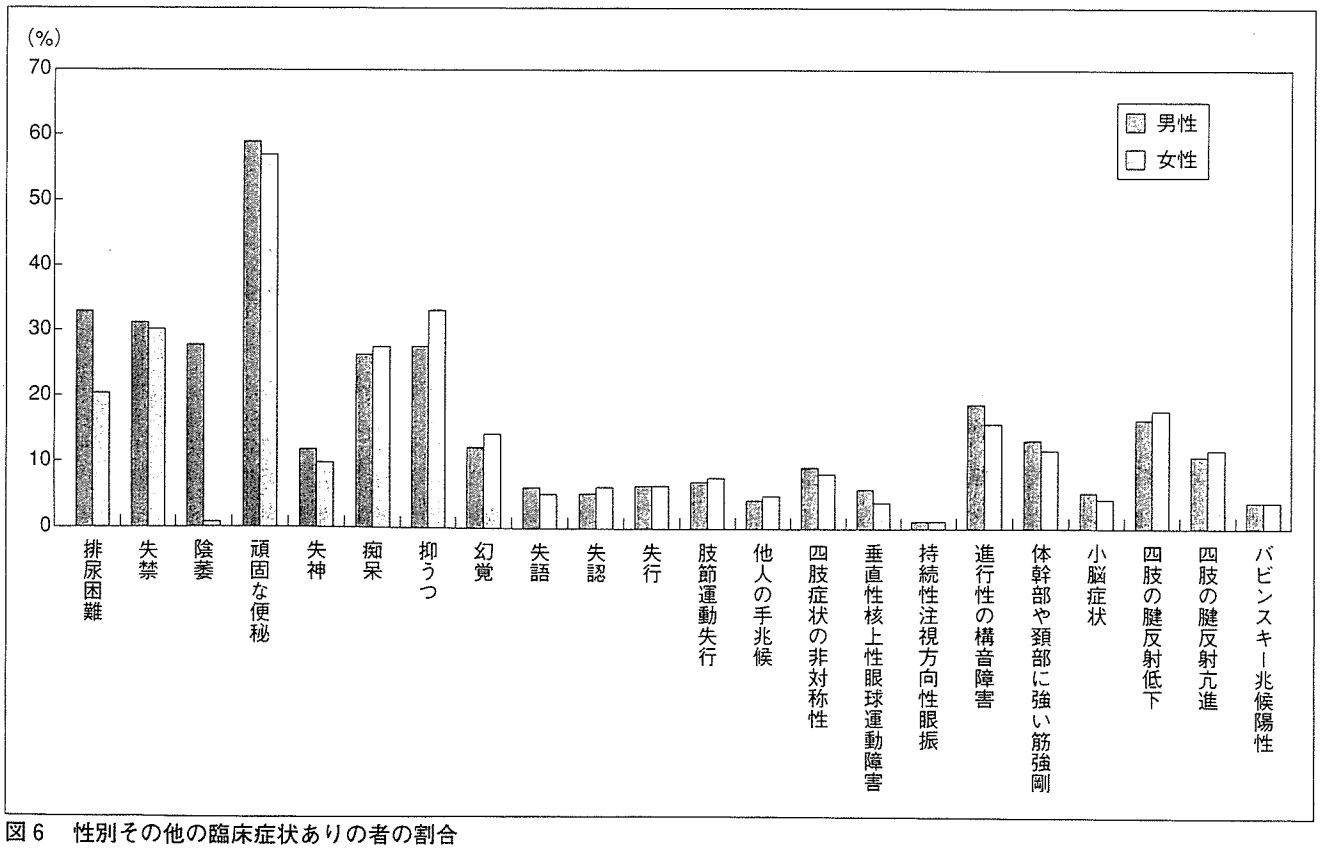

図6　性別その他の臨床症状ありの者の割合

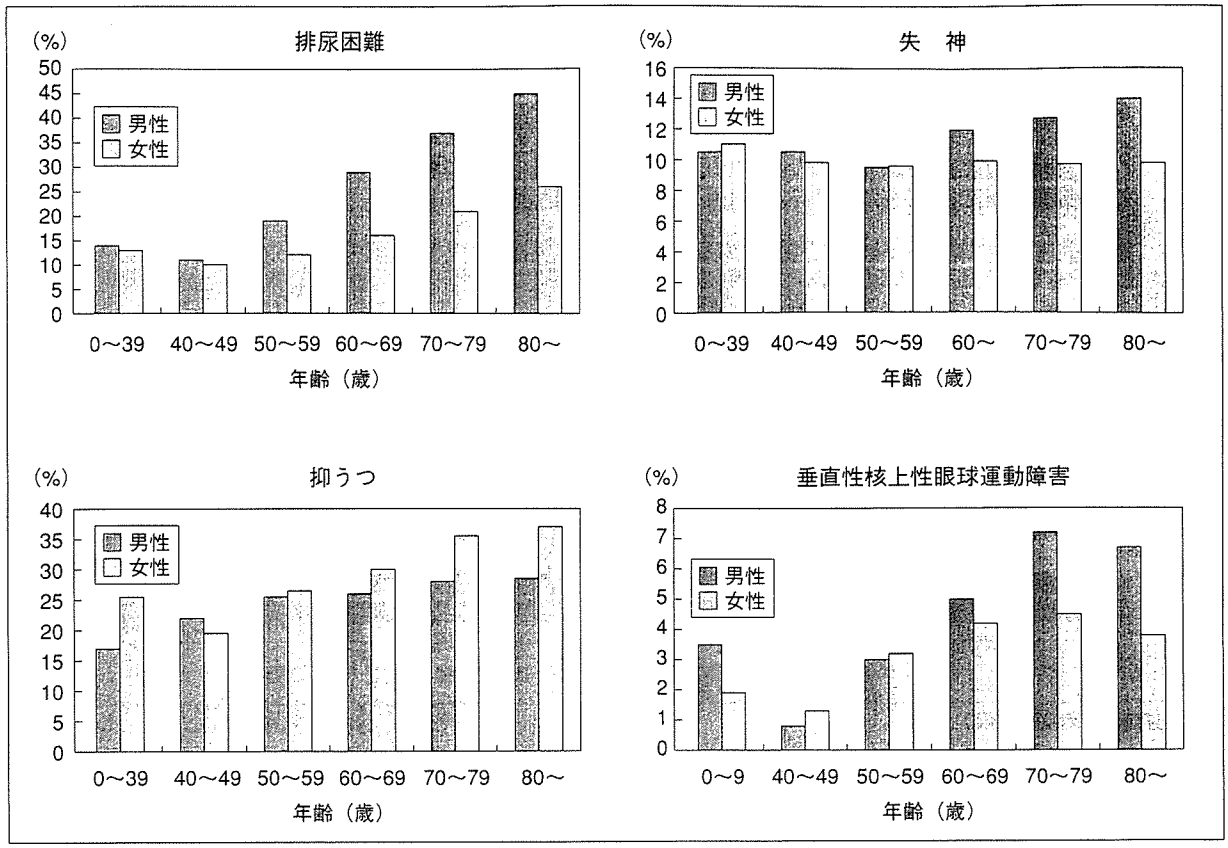

図7　性別年齢階級別その他の臨床症状ありの者の割合

差が明らかにできた。発病後期間は女性が男性よりやや長いが，発病後期間の違いがYahrの臨床重症度との性差に関係していた可能性が考えられる。

神経症状の頻度の性差については固縮，振戦，寡動について重症度の性差はなかったと報告されている[4]。今回の結果では立ち上がり，歩行，姿勢，姿勢安定性などで重症度が高いものが女性に多かった。

その他の自律神経症状や精神症状などの性差の報告は少ないが，嚥下障害や言語障害，膀胱障害では男性が高いという報告があった[3]。今回は，排尿困難，失神，進行性の構音障害，垂直性核上性眼球運動障害で男性が高く，抑うつで女性が高いという結果であった。性別年齢階級別にみると排尿困難は高齢の男性で高く，抑うつは高齢の女性で高くなっている。この結果は高年齢の患者において，男性で前立腺疾患による排尿困難や，女性でのうつ病による抑うつなど他の疾患によるものが含まれている可能性が考えられる。

パーキンソン病関連疾患の臨床像の性差について概説した。Yahrの臨床重症度や日常生活機能障害度で，神経症状の重症度，排尿困難，失神，抑うつなどのある者の割合で，性別に違いが見られた。

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Special Report

サルコイドーシスの臨床症状における性差

The Feature of Sarcoidosis: Sex Difference in Clinical Symptoms

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Key Words

サルコイドーシス（sarcoidosis），臨床調査個人票（clinical data of patients with intractable diseases receiving financial aid for treatment）

はじめに

サルコイドーシスは，原因不明の全身性疾患である。通常，若年成人，中年成人にみられ，しばしば両側性肺門リンパ節腫脹（BHL），肺浸潤，眼病変，皮膚病変を呈し，肝臓，脾臓，リンパ節，唾液腺，心臓，神経組織，筋，骨，また他の臓器が侵されることがある[1]。

わが国では，1974年10月に特定疾患治療研究対象疾患として医療費公費負担制度が適用されて以来，受給者数，病態や治療法などが明らかにされてきた。地域保健・老人保健事業報告[2]によると，2003年度の医療受給者数は，1万8,678人（男性5,386人，女性1万3,292人）で，やや女性に多い疾患である。患者の年齢分布は男女とも2峰性（20～30歳代と50～60歳代が高い）を示し，男性は若年の山の方が高く，女性は高年の山の方が高く，患者の年齢分布に性差があることが報告されている[3]。

本稿では，臨床調査個人票に含まれる情報のうち，受給者の性，年齢，臨床症状，検査所見，発見動機を用い，わが国のサルコイドーシスの受給者の臨床症状を明らかにし，その性差について概説する。

ところで，今回用いた臨床調査個人票は，2001年度より電子入力されるようになり，対象疾患すべてについて系統的にその情報を解析することが可能になったものである。2003年度に電子入力された臨床調査個人票は，受給者全体の50%弱であるが，入力状況には，性，年齢に大きな偏りは見られないため，疾患ごとの臨床症状についての検討が可能である[4]。なお本報告では，解析対象を2003年度受給者のうち比較的新しい症例が多い新規受給者（男性215人，女性369人）とした。

サルコイドーシスの新規受給者の性差

新規医療受給者の年齢分布は，男女とも2峰性を示

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し，男性は第１峰（20歳代），女性は第２峰（50歳代）の山が高い（図１）。

臨床症状の性差

自覚症状のある者は男性が女性より少なく，男性の45歳未満で特に少ない。自覚症状の種類をみると男女とも視力障害が最も多く，次いで咳，息切れなどの呼吸器症状が多い。自覚症状として視力障害のある者は，女性より男性で少なく，特に45歳未満の男性で少ない（図２）。

眼所見は，ぶどう膜炎，網膜所見，虹彩，隅角所見，視力障害ありの者などが比較的多くみられるが，これら眼所見は，女性で多く男性で少ない。特に45歳未満の男性でぶどう膜炎，網膜所見，視力障害などが少ない（図３）。

胸部所見は，肺門リンパ節腫脹ありの者が約80%，肺野びまん性陰影ありの者は約40～50%であるが，これらの所見は女性より男性に多く，特に45歳未満の男性で多い（図４）。

心臓所見は，心電図異常所見ありの者は，男性が女性より多く，特に45歳以上の男性で多い（図５）。心筋シンチ異常ありの者は，男性より女性に多く，特に45歳以上の女性に多い（図５）。

皮膚所見のある者は，女性に多く男性で少ない。特に結節や結節性紅斑などは45歳未満の男性で少ない（図６）。

サルコイド肉芽腫所見ありの者は，女性より男性にやや多く，特に45歳未満の男性に多い（図７）。血清アンジオテンシン変換酵素（ＡＣＥ）上昇所見ありの者の割合は，男女で大きな差はないが，45歳未満の女性でやや少ない（図７）。その他，ツベルクリン反応陰性所見，Ga集積陽性像や気管支肺胞洗浄液異常などは，45歳未満の男性で多い（図７，図８）。

発見動機は，男性では健康診断，女性では自覚症状によるものが多い。男性は健康診断が発見動機である者が多く，特に男性の45歳未満では，健康診断が48.0%と多い（図９）。

まとめ

サルコイドーシスの臨床症状の性差について概説した。女性に比べ，男性の特に若年者で胸部Ｘ線検査で把握される肺門リンパ節腫脹のある者が多く，自覚症状を持つ者，特に眼所見，皮膚所見など自覚症状に結びつく所見を持つ者が少なかった。発見動機は，男性で特に若年者で健康診断による者が多く，このような男性の若年者の臨床症状の特徴は，健康診断を発見動機として見つかるケースの特徴の反映と考えられた。

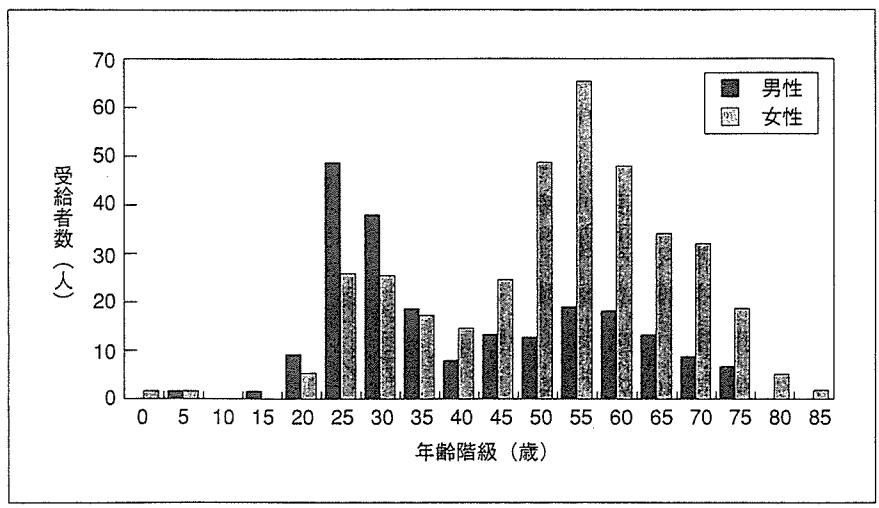

図１　2003年度新規受給者の性・年齢分布

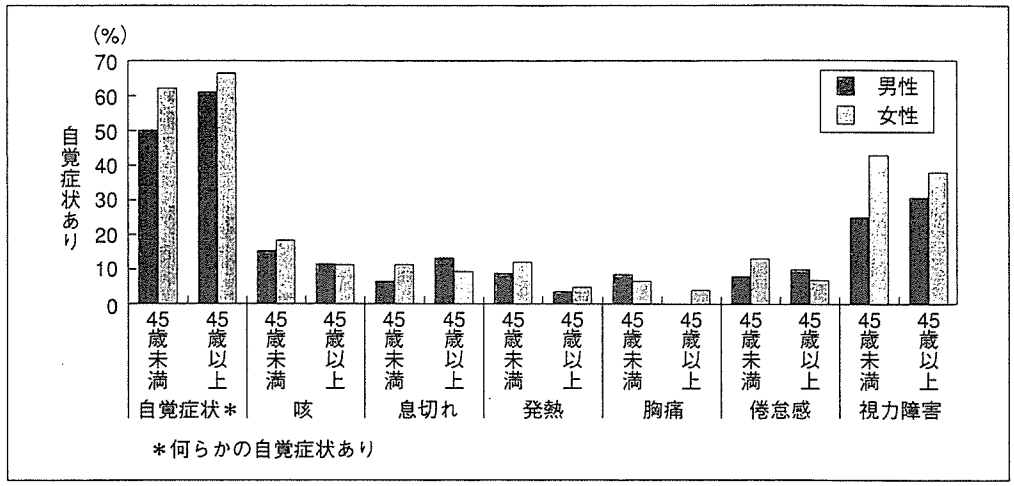

図2　自覚症状ありの者の割合，性別，年齢別

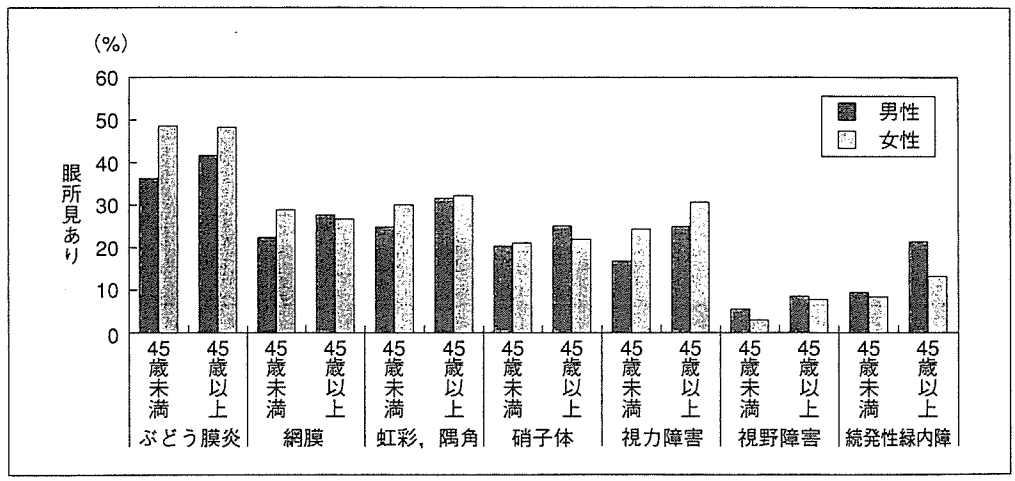

図3　眼所見ありの者の割合，性別，年齢別

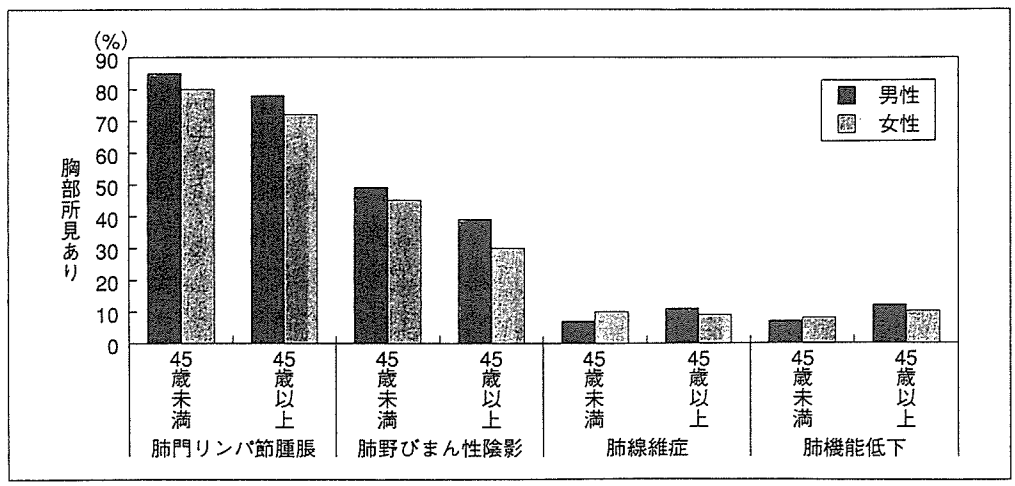

図4　胸部所見ありの者の割合，性別，年齢別

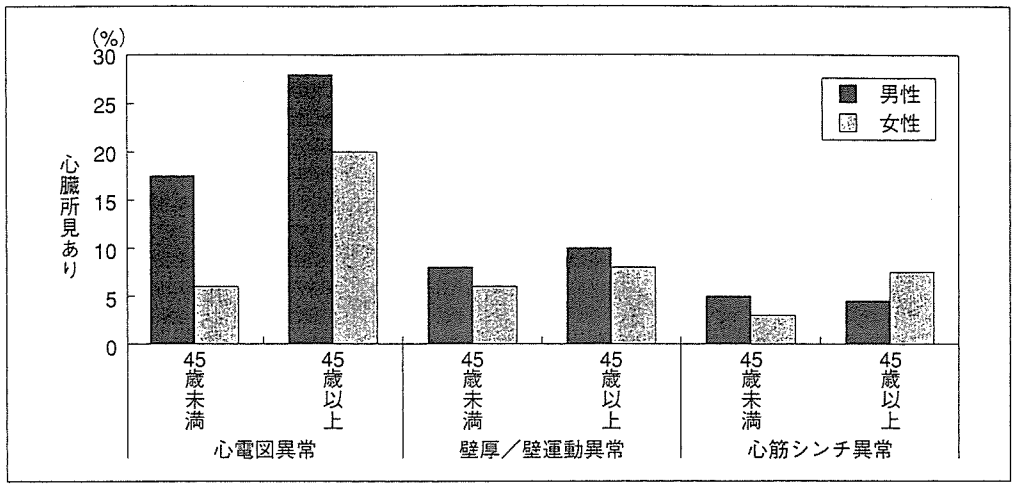

図5　心臓所見ありの者の割合，性別，年齢別

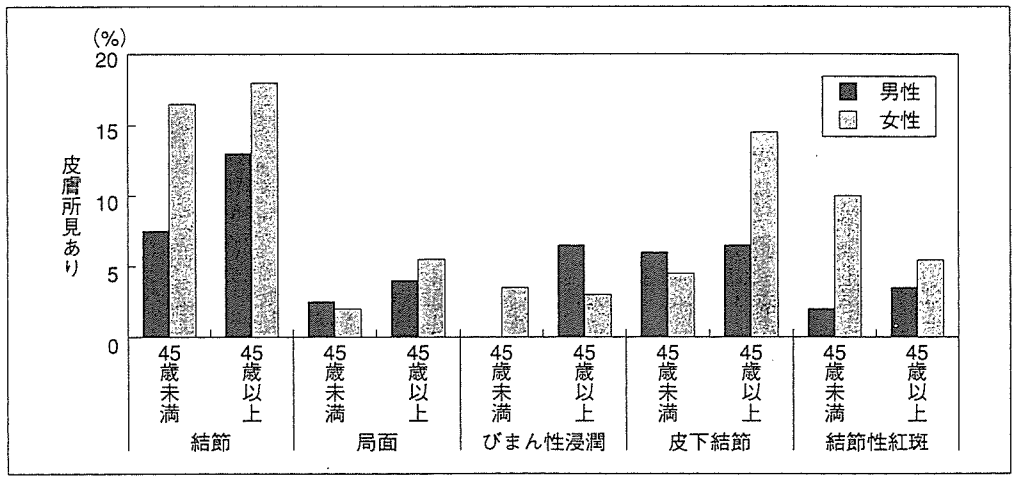

図6　皮膚所見ありの者の割合，性別，年齢別

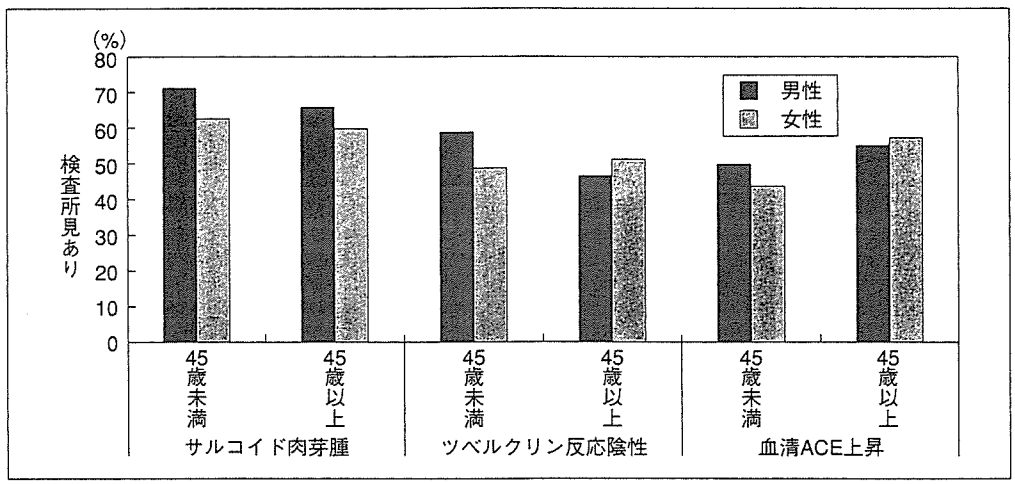

図7　検査所見ありの者の割合，性別，年齢別

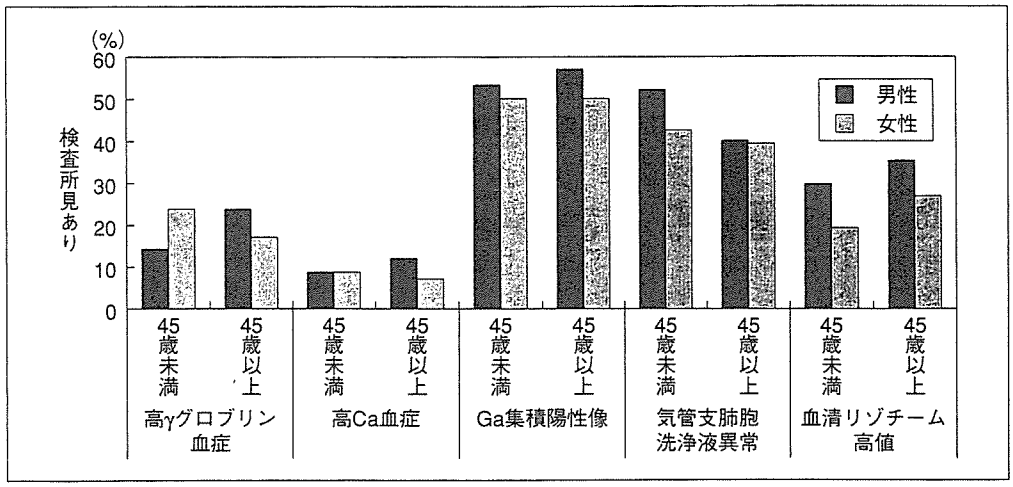

図8　検査所見ありの者の割合，性別，年齢別

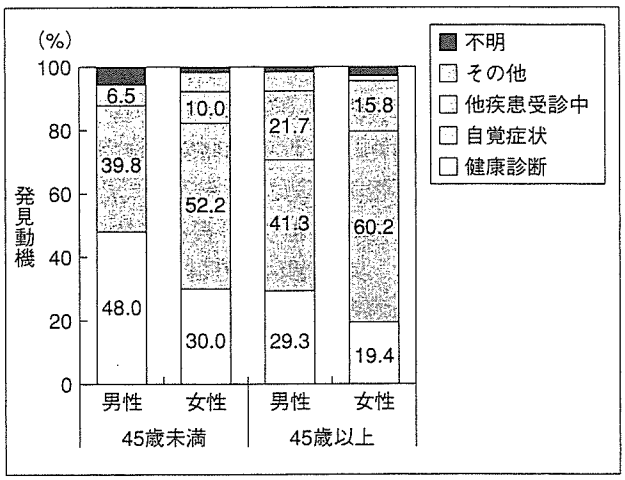

図9　発見動機の構成の割合，性別，年齢別

サルコイドーシスは，健診でBHLで発見される自覚症状の少ない疾患という印象もあるが，これは若年男性サルコイドーシスの特徴として顕著である。しかし，女性や高年の男性では，健診以外の自覚症状などで発見される者の割合が多く，眼症状，皮膚症状などを有する例が比較的多いことが明らかになった。

本稿は平成16年度厚生労働科学研究費補助金難治性疾患克服研究事業特定疾患の疫学に関する研究班による「電子入力された臨床調査個人票に基づく特定疾患治療研究医療受給者調査報告書」[4]の一部をまとめたものである。

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Original Article

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A scoring system to predict renal outcome in IgA nephropathy: from a nationwide prospective study

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Abstract

Background. Immunoglobulin A (IgA) nephropathy is the most common form of glomerulonephritis in the world, and a substantial number of patients develop end-stage renal disease (ESRD). Although there are several prognostic indicators, it remains difficult to predict the renal outcome in individual patients.

Methods. A prospective cohort study was conducted in 97 clinical units in Japan from 1995 to 2002. We analysed the data from 2269 patients using proportional hazards models in order to determine the predictors of ESRD in IgA nephropathy and to develop a scoring system to estimate ESRD risk.

Results. During the follow-up (median, 77 months), 207 patients developed ESRD. Systolic hypertension, proteinuria, hypoproteinaemia, azotaemia and a high histological grade at initial renal biopsy were independently associated with the risk of ESRD. Mild haematuria predisposed patients to ESRD more than severe haematuria. A scoring system was developed to estimate the 7-year ESRD risk from eight clinical and pathological variables. Actually, this prognostic score accurately classified patients by risk: patients with estimates of 0.0–0.9, 1.0–4.9, 5.0–19.9, 20.0–49.9, and 50.0–100.0% had a 0.2, 2.4, 12.2, 40.2 and 80.8% of ESRD incidence over 7 years, respectively. The corresponding area under the receiver operating characteristic curve was 0.939 [95% confidence interval (CI), 0.921–0.958]. This score was verified in repetitions of the derivation-validation technique.

Conclusions. Although the quality of some data collected by the mail survey is limited and the influence of therapy could not be considered, this scoring system will serve as a useful prognostic tool for IgA nephropathy in clinical practice.

Keywords: end-stage renal disease; IgA nephropathy; kidney failure; prospective studies; renal prognosis

Introduction

Immunoglobulin A (IgA) nephropathy is the most common form of glomerulonephritis in the world today [1]. When Berger and Hinglais [2] described this disease as a new clinical entity in 1968, clinicians regarded it as a benign nephropathy. However, successive studies indicated that 6–43% of IgA nephropathy patients would develop end-stage renal disease (ESRD) over a period of 10 years [3,4].

Many investigators have tried to determine the prognostic indicators of this disease, which include elevated serum creatinine (sCr), heavy proteinuria, severe histological changes, hypertension, hypoproteinaemia, older age and male sex [4–7].

However, difficulties remain in predicting the renal outcomes in individual patients and determining those who need aggressive therapeutic intervention. This may be partly a result of the relatively small sample sizes used in previous studies [8]. We, therefore, set up a large-scale, nationwide prospective study in order to develop an IgA nephropathy prognostic score.

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Subjects and methods

Patients and follow-up

The Research Group on Progressive Renal Diseases and the Research Committee on the Epidemiology of Intractable Diseases, both organized by the former Ministry of Health and Welfare of Japan (currently the Ministry of Health, Labor and Welfare), conducted a nationwide survey on IgA nephropathy in January 1995 [9]. This survey identified 5324 patients with biopsy-proven IgA nephropathy, who had visited general physicians, nephrologists, paediatricians or urologists in Japan during 1994.

Follow-up was carried out at clinical units that had 10 or more IgA nephropathy patients in the survey. When more than 50 of them were identified in a unit, we randomly selected 50 to reduce the burden on the unit. We eventually designated 3409 patients as potential subjects for the follow-up study and undertook the first mail survey in May 1997. The response rate was 82.5% in a patient base. A second mail survey was conducted for 2350 cases in August 1999, and a third for 2285 cases in November 2002, with response rates of 95.7 and 93.3%, respectively. Excluding those who had died, who had developed ESRD before baseline, or whose essential baseline data were missing, we included 2269 eligible patients for the analyses from 97 clinical units. Figure 1 shows their distribution by sex and age. There are two peaks in age distribution: 15–24 and 40–49 years. The median follow-up period was 77 months (range, 1–94 months).

This investigation was approved by the Ethics Committee of the Kyoto University Graduate School of Medicine and the Ethics Committee of the Juntendo University School of Medicine.

Data collection

The baseline data of the patients were obtained by reviewing medical records in the nationwide survey in 1995. The data included sex, age, year of diagnostic renal biopsy, systolic and diastolic blood pressure, urine protein and blood, serum total protein and albumin and sCr. Proteinuria was semi-quantified with a standard urine dipstick with (−), (+−), (+), (++) and (+++) corresponding to <10, 10–29, 30–99, 100–299 and ≥300 mg/dl of urine albumin, respectively. Histological grade at initial renal biopsy was reassessed by pathologists or nephrologists in each participating hospital at the first follow-up survey using the new criteria from the Joint Committee of the Research Group on Progressive Renal Diseases and the Japanese Society of Nephrology (Table 1) [10]. This reassessment was needed because the classification criteria were established after our baseline survey. In the three follow-up surveys, information on outcomes such as death, ESRD and sCr was collected by mail.

Statistical analysis

Predictors of ESRD. The primary endpoint in this study was ESRD, which was defined as the initiation of dialysis therapy. The follow-up period for each patient was calculated in months from the data of the nationwide survey on ESRD, death or the last visit. Those who died without ESRD were treated as censored cases.

The 7-year cumulative incidence (risk) of ESRD was computed by the Kaplan–Meier method [11] according to demographic and clinical characteristics. The rate ratios (RRs)

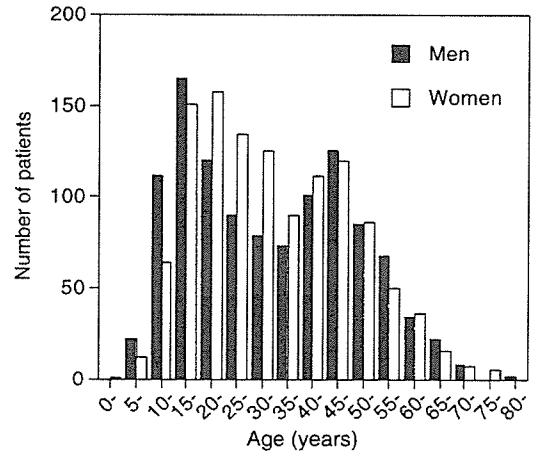

Fig. 1. Sex and age distribution of patients (1104 men and 1165 women) for analysis.

Table 1. Criteria for histological grading from the Joint Committee of the Research Group on Progressive Renal Diseases (Ministry of Health and Welfare of Japan), and the Japanese Society of Nephrology [10]

Grade	Glomerular findings	Interstitial and vascular findings
I	Slight mesangial cell proliferation and increased matrix. Glomerulosclerosis, crescent formation or adhesion to the Bowman's capsule is not observed.	Prominent changes are not seen in the interstitium, renal tubuli or blood vessels.
II	Slight mesangial cell proliferation and increased matrix. Glomerulosclerosis, crescent formation or adhesion to the Bowman's capsule seen in <10% of all biopsied glomeruli.	Same as above.
III	Moderate, diffuse mesangial cell proliferation and increased matrix. Glomerulosclerosis crescent formation or adhesion to the Bowman's capsule seen in 10–30% of all biopsied glomeruli.	Cellular infiltration is slight in the interstitium except around some sclerosed glomeruli. Tubular atrophy is slight, and mild vascular sclerosis is observed.
IV	Severe, diffuse mesangial cell proliferation and increased matrix. Glomerulosclerosis, crescent formation or adhesion to the Bowman's capsule seen in >30% of all biopsied glomeruli. When sites of sclerosis are totalled and converted to global sclerosis, the sclerosis rate is >50% of all glomeruli. Some glomeruli also show compensatory hypertrophy. The sclerosis rate is the most important of these indices.	Interstitial cellular infiltration and tubular atrophy, as well as fibrosis are seen. Hyperplasia or degeneration may be seen in some intrarenal arteriolar walls.

for ESRD were estimated by potential prognostic factors using proportional hazards models [12]. The independent effect of each variable was assessed by multivariate analysis. Diastolic blood pressure and serum albumin were excluded from the multivariate model because of their close relation with systolic blood pressure and serum total protein, respectively. To test for a linear trend, we coded each stratum of the variable as 0, 1, 2,... and included it as a continuous variable in the proportional hazards model [13]. For variables that displayed 'U-shape' or 'inverted U-shape' relationships with ESRD risk, we also analysed non-linear associations using a quadratic model [14]. Subjects with missing values were omitted from the relevant analysis.

Construction of scoring system. A scoring system to predict ESRD in individual patients with IgA nephropathy was based on the proportional hazards model. It included sex, age and all the significant variables in the aforementioned multivariate analysis. In this model, a patient with covariate values $X_1, X_2, \ldots, X_n$ has an expected renal survival rate (= 1 − cumulative incidence of ESRD) at time t, $S(t)$, formulated as:

$$S(t) = \{S_0(t)\}^{\exp(\beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_n X_n)}$$

where $S_0(t)$ is the baseline survivor function and $\beta_1, \beta_2, \ldots, \beta_n$ are the coefficients estimated from the model [8,15]. The RRs are exponents of these β coefficients.

We stratified the patients by each prognostic factor and applied a proportional hazards model with dummy variables (0 or 1 for $X_1, X_2, \ldots, X_n$). The scores derived from the β coefficients were smoothed by linear interpolation in each stratum of the variables and were then multiplied by 10 to simplify the calculation. The sum of all the scores for individual factors (total score) was $10 \times (\beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_n X_n)$, and a corresponding ESRD risk, $1 - S(t)$, was computed from the total score. The baseline survivor function, $S_0(t)$, was estimated by the product-limit method using the PHREG procedure of the Statistical Analysis System [16].

Validation of scoring system. To examine the goodness of fit of the scoring system to the data, we divided the patients into five groups according to the predicted 7-year risk of ESRD, that is, minimum (0.0–0.9%), low (1.0–4.9%), moderate (5.0–19.9%), high (20.0–49.9%) and very high (50.0–100.0%). The renal survival curve of ESRD was then drawn in each group using the Kaplan–Meier method [11]. To further assess the utility of the score, we used the area under the receiver operating characteristic (ROC) curve [17] for the 7-year risk of ESRD. The area and its 95% confidence interval (CI) were estimated by the non-parametric method [17].

As an additional analysis [18], one-third ($n = 756$) of the subjects were randomly allocated to a validation sample and the remainder to a derivation sample. The prognostic score was developed in the derivation sample, and the actual 7-year cumulative incidence of ESRD was computed by the predicted risk in the validation sample [11]. The area under the ROC curve was also estimated in the validation group. Considering the sampling error, we repeated this procedure in 100 different validation sets. Smoothing of the scores was not done in this analysis.

Results

During the follow-up of 11 923.5 person-years, 207 patients with IgA nephropathy developed ESRD. Sixteen deaths without ESRD were also reported: five from circulatory diseases, five from cancer and six from unknown causes.

Table 2 summarizes the 7-year cumulative incidence and RR for ESRD by demographic and clinical factors. Patients with no or only mild proteinuria [urine protein of (−) or (+−)] had an appreciably lower risk of ESRD: their 7-year cumulative incidence was 0.7% (95% CI, 0.0–1.5%). In contrast, patients with excretional impairment at baseline had a much higher risk. Their 7-year cumulative incidences were 68.5% (95% CI, 59.2–77.8%) and 90.1% (82.4–97.8%) for sCr of 1.68–2.50 and ≥2.51 mg/dl (148–221 and ≥222 μmol/l), respectively. The proportion was as high as 25.9% (95% CI, 19.2–32.6%) even among those with mild azotaemia [sCr, 1.26–1.67 mg/dl (112–147 μmol/l)]. A univariate analysis with proportional hazards models revealed that earlier renal biopsy, systolic/diastolic hypertension, proteinuria, hypo-proteinaemia/albuminaemia, azotaemia and a higher histological grade at initial renal biopsy had a strong dose-dependent association with the risk of ESRD. Systolic hypertension, proteinuria, hypoproteinaemia, azotaemia and a higher histological grade remained significant predictors in the multivariate analysis (trend $P < 0.05$).

Although male patients had a higher RR in the univariate analysis, the high risk disappeared when considering other factors. Patients in their 30s were at the lowest risk in the multivariate analysis, whereas an upward trend in RR with advancing age was found in the univariate model. Mild haematuria [<30 red blood cells per high-power field (RBC/HPF)] was associated with a higher risk compared with severe haematuria (≥30 RBC/HPF) in both the univariate and multivariate analyses. In the multivariate models, we found a significant non-linear association of haematuria with ESRD risk (P for non-linear association <0.0001) but none for age ($P = 0.26$).

Based on these analyses, we established a scoring system to estimate 4- and 7-year cumulative incidence rates of ESRD. Of the 2269 patients included in this study, 1754 (77.3%) had a complete data set needed for our system designing. Table 3 lists the scores of individual prognostic factors. The total score (sum of individual scores) can then be converted to the corresponding estimated risk using Table 4. The baseline survivor function, $S_0(t)$, was estimated as 0.99955026 and 0.99887700 at 4 and 7 years, respectively. An illustrative example of how to apply this scoring system to patients with IgA nephropathy follows. The patient is a 59-year-old man with systolic blood pressure of 142 mmHg, proteinuria of (++), haematuria of ≥30 RBC/HPF, serum total protein of 6.6 g/dl, histological grade of IV at initial renal biopsy, and sCr of 1.35 mg/dl. As shown in Table 3, the scores

Table 2. Seven-year cumulative incidence and RRs for ESRD by demographic and clinical characteristics (at baseline except for histological grade)

	n	Observed person-years	No. of ESRD	7-year cumulative incidence of ESRD		RR for ESRD			
				%	95% CI	Univariate		Multivariate	
						RR	95% CI	RR	95% CI
Sex									
Female	1165	6315.2	76	8.2	6.3–10.0	1.00		1.00	
Male	1104	5608.3	131	15.2	12.7–17.7	1.93	1.46–2.57 $P<0.0001$	0.75	0.51–1.09 $P=0.13$
Age (years)									
≤19	526	2526.5	10	2.9	1.0–4.8	1.00			1.00
20–29	500	2475.4	32	8.7	5.8–11.7	3.29	1.62–6.70	1.28	0.51–3.24
30–39	367	2041.5	29	9.4	6.1–12.6	3.66	1.79–7.52	0.63	0.24–1.64
40–49	456	2601.6	57	14.7	11.1–18.2	5.67	2.89–11.1	0.73	0.29–1.80
50–59	289	1570.1	53	20.6	15.4–25.8	8.70	4.43–17.1	0.80	0.32–1.99
≥60	131	708.4	26	23.3	15.3–31.4	9.44	4.55–19.6	0.76	0.29–2.04
						trend $P<0.0001$		trend $P=0.41$	
Year of initial renal biopsy									
1994–1995	479	2525.8	31	8.5	5.5–11.5	1.00		1.00	
1992–1993	594	3059.0	54	12.2	9.1–15.4	1.44	0.92–2.23	1.30	0.74–2.27
1990–1991	402	2050.5	41	12.4	8.8–16.0	1.62	1.02–2.58	1.75	0.98–3.12
1988–1989	287	1609.4	26	10.4	6.4–14.4	1.32	0.78–2.22	1.31	0.69–2.48
1987 or before	469	2450.1	53	14.2	10.5–17.8	1.76	1.13–2.74	1.21	0.69–2.13
						trend $P=0.033$		trend $P=0.60$	
Systolic blood pressure (mmHg)									
≤119	812	4259.8	26	4.6	2.8–6.4	1.00		1.00	
120–139	845	4577.9	79	11.5	9.0–14.0	2.84	1.82–4.42	1.32	0.79–2.23
140–159	344	1785.4	63	22.3	17.3–27.2	5.79	3.67–9.15	1.43	0.82–2.49
≥160	70	298.4	21	33.9	21.9–45.9	11.5	6.48–20.5	2.62	1.33–5.18
						trend $P<0.0001$		trend $P=0.014$	
Diastolic blood pressure (mmHg)									
≤69	663	3399.3	15	3.2	1.5–4.8	1.00			
70–79	594	3205.7	40	9.4	6.5–12.2	2.85	1.58–5.16		
80–89	516	2831.0	67	15.1	11.7–18.5	5.41	3.09–9.48		
90–99	231	1163.8	55	27.3	21.0–33.6	10.8	6.08–19.0		
≥100	66	316.7	12	21.6	10.6–32.7	8.65	4.05–18.5		
						trend $P<0.0001$			
Proteinuria									
(−), (±)	827	4284.8	4	0.7	0.0–1.5	1.00		1.00	
(+)	528	2952.8	25	6.4	3.9–8.9	9.12	3.18–26.2	2.97	0.86–10.3
(++)	484	2557.5	73	18.3	14.4–22.2	30.7	11.2–83.8	7.41	2.23–24.6
(+++)	330	1619.2	89	30.9	25.4–36.5	58.7	21.6–160	11.0	3.28–36.6
						trend $P<0.0001$		trend $P<0.0001$	
Haematuria (red blood cells per high-power field)									
None	578	2949.7	20	4.9	2.7–7.0	1.00		1.00	
1–29	1238	6531.3	147	14.7	12.4–17.0	3.33	2.09–5.31	3.65	2.02–6.60
≥30	363	1979.5	24	7.9	4.8–10.9	1.80	0.99–3.25	1.37	0.65–2.89
						trend $P=0.024$		trend $P=0.58$	
Serum total protein (g/dl)									
≥7.5	448	2385.7	11	3.7	1.5–5.9	1.00		1.00	
7.0–7.4	758	3991.8	43	7.7	5.5–10.0	2.33	1.20–4.52	1.50	0.67–3.33
6.5–6.9	678	3663.8	69	12.6	9.7–15.4	4.08	2.16–7.71	1.71	0.79–3.71
6.0–6.4	243	1228.2	50	23.9	17.8–29.9	8.78	4.57–16.9	1.71	0.77–3.76
≤5.9	76	349.8	28	40.2	28.4–52.0	17.3	8.61–34.7	3.20	1.33–7.74
						trend $P<0.0001$		trend $P=0.019$	
Serum albumin (g/dl)									
≥4.4	822	4289.0	27	4.8	3.0–6.7	1.00			
4.2–4.3	434	2341.0	21	6.7	3.9–9.6	1.43	0.81–2.53		
4.0-4.1	360	2042.5	38	12.3	8.5–16.0	2.98	1.82–4.87		
3.8-3.9	228	1204.5	36	18.2	12.6–23.7	4.75	2.89–7.83		
≤3.7	227	1110.7	70	34.7	27.9–41.5	10.0	6.41–15.6		
						trend $P<0.0001$			
1/sCr $[(mg/dl)^{-1}$, numbers in parentheses indicate sCr (mg/dl)$]$[a]									
≥0.80 (≤1.25)	1881	10197.3	32	2.5	1.6–3.4	1.00		1.00	
0.60–0.79 (1.26–1.67)	205	1142.0	45	25.9	19.2–32.6	12.6	7.99–19.8	6.62	3.62–12.1

Continued

Table 2. Continued

	n	Observed person-years	No. of ESRD	7-year cumulative incidence of ESRD		RR for ESRD			
				%	95% CI	Univariate		Multivariate	
						RR	95% CI	RR	95% CI
0.40–0.59 (1.68–2.50)	113	464.3	70	68.5	59.2–77.8	49.6	32.6–75.4	23.6	13.1–42.4
≤0.39 (≥2.51)	70	120.0	60	90.1	82.4–97.8	175	113–272	110	56.1–215
						trend $P < 0.0001$		trend $P < 0.0001$	
Histological grade at initial renal biopsy									
Grade I	514	2591.1	8	2.7	0.8–4.7	1.00		1.00	
Grade II	698	3772.5	21	3.9	2.2–5.6	1.81	0.80–4.09	0.89	0.34–2.33
Grade III	688	3822.7	83	14.4	11.4–17.4	7.07	3.42–14.6	1.69	0.71–4.04
Grade IV	212	954.3	80	43.2	35.9–50.6	27.1	13.1–56.0	2.57	1.04–6.33
						trend $P < 0.0001$		trend $P = 0.0007$	

ESRD, end-stage renal disease; CI, confidence interval; RR, rate ratio; sCr, serum creatinine.
[a]To convert the values of creatinine to μmol/l, multiply by 88.4.

for sex, age, systolic blood pressure, proteinuria, haematuria, serum total protein, histological grade and sCr are −2, −3, 3, 20, 3, 5, 9 and 11, respectively. Thus, the total score is calculated to be 46 [(−2) + (−3) + 3 + 20 + 3 + 5 + 9 + 11]. Using Table 4, this total score of 46 can be converted to a 4- and 7-year ESRD risk of 4.4 and 10.6%, respectively.

The actual renal survival (= 1 − cumulative incidence of ESRD) according to the estimated 7-year risk was plotted in Figure 2. The prognostic score successfully classified the patients by risk. Those with an estimated risk of 0.0–0.9% (score, −8 to 21), 1.0–4.9% (22–38), 5.0–19.9% (39–52), 20.0–49.9% (53–64) and 50.0–100.0% (65 or more) had an actual cumulative incidence of ESRD in 7 years of 0.2% (95% CI, 0.0–0.7%), 2.4% (0.8–3.9%), 12.2% (7.2–17.3%), 40.2% (27.7–52.6%) and 80.8% (73.3–88.3%), respectively. This showed good agreement between the estimated and observed risks.

The corresponding area under the ROC curve was 0.939 (95% CI, 0.921–0.958). The area remained almost the same when the prognostic scores were not smoothed by linear interpolation (0.947; 95% CI, 0.930–0.964).

The influence of therapy could not be taken into account in the scoring system, because data on treatment were not collected at baseline and only the history of use (yes or no) of six groups of drugs (antiplatelet agents, corticosteroids, immunodepressants, angiotensin-converting enzyme inhibitors, calcium channel blockers and fish oil, and others) [19,20] at the 1997 survey was available for most of the cases. The drugs had been used for 82.2, 35.3, 10.9, 29.2, 20.0 and 34.1% of the patients, respectively, until the 1997 survey. Additional multivariate analyses that included the history of drug use did not essentially alter the associations of clinical characteristics with the ESRD risk presented in Table 2, except for the attenuation of risk for systolic blood pressure (data not shown).

Even when the prognostic scores were developed using derivation samples randomly selected from all subjects, the estimated 7-year cumulative incidence of ESRD well-predicted the observed ones in the remaining validation sample. The median values of observed 7-year incidence were 0.5% [inter-quartile range (IQR), 0.0–0.8%], 2.2% (1.3–3.0%), 12.9% (10.0–16.2%), 39.5% (32.9–44.6%) and 75.3% (70.7–79.7%) in patients with an estimated risk of 0.0–0.9, 1.0–4.9, 5.0–19.9, 20.0–49.9 and 50.0–100.0%, respectively. The median of the corresponding area under the ROC curve (0.927; IQR, 0.913–0.941) was comparable with the area in the full data set (0.939).

Discussion

Based on a large-scale cohort study, we described the prognostic indicators for IgA nephropathy and developed a scoring system for estimating the ESRD risk. Systolic hypertension, proteinuria, haematuria, hypoproteinaemia, azotaemia and a high histological grade at initial renal biopsy were related to the risk, independent of other factors. The prognostic score successfully classified patients according to their ESRD risk and was verified by the analysis, dividing the subjects into derivation and validation samples.

To the best of our knowledge, this is the largest follow-up study to date on the renal outcome of IgA nephropathy. The present investigation enrolled many IgA nephropathy patients at various clinical stages, which enabled us to quantify ESRD risk by prognostic factors in detail. Whereas most studies to date followed IgA nephropathy patients from the time of initial renal biopsy or diagnosis [4], our study included patients at different stages. Therefore, the prognostic score can be applied appropriately whenever needed. Use of clinical data subsequent to renal biopsy may improve the prediction of renal outcome [4].

Table 3. Prognostic scores to estimate risk of ESRD by demographic and clinical factors

Sex		Age (years)		SBP (mmHg)	
Sex	Score	Age	Score	SBP	Score
Female	0	≤21	0	≤121	0
Male	−2	22–23	1	122–124	1
		24–26	2	125–127	2
		27	1	128–144	3
		28	0	145–151	4
		29–30	−1	152	5
		31	−2	153–154	6
		32–33	−3	155	7
		34	−4	156–157	8
		35–38	−5	158	9
		39–46	−4	≥159	10
		47–53	−3		
		54–58	−2		
		≥59	−3		

Proteinuria		Haematuria (RBC/HPF)		Serum TP (g/dl)		Histological grade[a]	
Proteinuria	Score	Haematuria	Score	TP	Score	Grade	Score
(−), (+−)	0	None	0	≥7.5	0	Grade I	0
(+)	11	1–29	12	7.4	2	Grade II	−1
(++)	20	≥30	3	7.3	3	Grade III	6
(+++)	24			6.9–7.2	4	Grade IV	9
				6.3–6.8	5		
				6.2	6		
				6.1	9		
				≤6.0	12		

Serum creatinine (mg/dl)[b]

Creatinine	Score	Creatinine	Score	Creatinine	Score	Creatinine	Score
≤1.25	0	1.37	13	1.66–1.69	25	2.15–2.17	37
1.26	1	1.38	14	1.70–1.73	26	2.18–2.20	38
1.27	2	1.39	15	1.74–1.78	27	2.21–2.23	39
1.28	3	1.40	16	1.79–1.83	28	2.24–2.26	40
1.29	5	1.41	17	1.84–1.88	29	2.27–2.30	41
1.30	6	1.42–1.43	18	1.89–1.94	30	2.31–2.33	42
1.31	7	1.44–1.46	19	1.95–2.00	31	2.34–2.37	43
1.32	8	1.47–1.50	20	2.01–2.02	32	2.38–2.41	44
1.33	9	1.51–1.53	21	2.03–2.05	33	2.42–2.45	45
1.34	10	1.54–1.57	22	2.06–2.08	34	2.46–2.49	46
1.35	11	1.58–1.61	23	2.09–2.11	35	≥2.50	47
1.36	12	1.62–1.65	24	2.12–2.14	36		

SBP, systolic blood pressure; RBC/HPF, red blood cells per high-power field; TP, total protein.
[a]Histological grade at initial renal biopsy.
[b]To convert the values of creatinine to μmol/l, multiply by 88.4.

As expected from previous studies [3–7], hypertension, proteinuria, hypoproteinaemia, higher sCr and more severe morphological changes were independent risk factors for ESRD. Mild haematuria (<30 RBC/HPF) was related to a higher risk of ESRD than the more severe type (≥30 RBC/HPF). This supports the clinical impression that gross haematuria is a good sign [8], although the association still remains controversial [4] and its mechanism not yet fully understood. The reproducibility of severe haematuria was not so high as that of proteinuria. The potential misclassification, if any, will attenuate the actual difference in ESRD risk between the groups of mild and severe haematuria. Considering repeated measures of haematuria may serve to further clarify the poor prognosis associated with mild haematuria.

The lower the glomerular filtration rate (GFR) of a patient reflected in higher sCr, the sooner the patient will reach ESRD if the rate of decline in GFR is the same.

Male patients were at an increased risk of ESRD in the univariate analysis, but that finding disappeared

Table 4. Estimated 4- and 7-year risk of ESRD by total score

Total score	Estimated risk (%)		Total score	Estimated risk (%)		Total score	Estimated risk (%)		Total score	Estimated risk (%)	
	4-year	7-year		4-year	7-year		4-year	7-year		4-year	7-year
(-8)-0	0.0	0.1	25	0.5	1.4	50	6.5	15.4	75	55.7	86.9
1	0.0	0.1	26	0.6	1.5	51	7.1	16.8	76	59.3	89.4
2	0.1	0.1	27	0.7	1.7	52	7.8	18.4	77	63.0	91.6
3	0.1	0.2	28	0.7	1.8	53	8.6	20.2	78	66.6	93.6
4	0.1	0.2	29	0.8	2.0	54	9.5	22.0	79	70.3	95.2
5	0.1	0.2	30	0.9	2.2	55	10.4	24.0	80	73.8	96.5
6	0.1	0.2	31	0.99	2.5	56	11.5	26.2	81	77.3	97.5
7	0.1	0.2	32	1.1	2.7	57	12.6	28.5	82	80.6	98.3
8	0.1	0.2	33	1.2	3.0	58	13.8	31.0	83	83.6	98.9
9	0.1	0.3	34	1.3	3.3	59	15.1	33.6	84	86.5	99.3
10	0.1	0.3	35	1.5	3.7	60	16.6	36.4	85	89.0	99.6
11	0.1	0.3	36	1.6	4.0	61	18.2	39.4	86	91.3	99.8
12	0.1	0.4	37	1.8	4.4	62	19.9	42.5	87	93.3	99.9
13	0.2	0.4	38	2.0	4.9	63	21.7	45.8	88	94.9	99.9
14	0.2	0.5	39	2.2	5.4	64	23.7	49.1	89	96.3	100
15	0.2	0.5	40	2.4	6.0	65	25.9	52.6	90	97.4	100
16	0.2	0.6	41	2.7	6.6	66	28.2	56.2	91	98.2	100
17	0.2	0.6	42	3.0	7.2	67	30.6	59.9	92	98.8	100
18	0.3	0.7	43	3.3	7.9	68	33.2	63.5	93	99.3	100
19	0.3	0.7	44	3.6	8.7	69	36.0	67.2	94	99.6	100
20	0.3	0.8	45	4.0	9.6	70	38.9	70.8	95	99.8	100
21	0.4	0.9	46	4.4	10.6	71	42.0	74.4	96	99.9	100
22	0.4	1.0	47	4.8	11.6	72	45.3	77.8	97	99.9	100
23	0.4	1.1	48	5.3	12.8	73	48.6	81.0	98	100	100
24	0.5	1.2	49	5.9	14.0	74	52.1	84.1	99–116	100	100

in the multivariate model. The sCr level is essentially higher in men than in women due to the greater production of creatinine in males [21]. Nevertheless, the decision when to start haemodialysis is made mainly based on the sCr level irrespective of sex. Thus, male sex would seemingly be a risk factor for ESRD. In fact, it was not a risk factor after adjustment for sCr, but the elevated risk among men appeared again in the proportional hazards model excluding 1/sCr (RR, 1.49; 95% CI, 1.05–2.10).

A U-shaped association was found between age and ESRD risk after adjustment for other prognostic factors, though the non-linear association was not statistically significant. Age was positively associated with the ESRD risk in previous univariate analyses [4], whereas negative associations were observed in preceding multivariate ones [7,22]. Most of these studies treated age as a single continuous variable in the multivariate model. Our 10-year stratification of age revealed a possible non-linear relationship.

We proposed a new scoring system for the prediction of renal outcome in individual IgA nephropathy patients. Compared with several previous studies providing prognostic measures according to clinico-pathological factors, our system has some advantages in terms of background data and target outcome. First, it is based on the data from a much larger sample than the one in a previous study by Beukhof *et al.* [8]. Second, it predicts the risk of ESRD, rather than that of surrogate endpoints such as an increase in sCr [15]. Although D'Amico and coworkers [23] developed a scoring index using proteinuria and three histological variables, and Frimat and colleagues [24] developed a classification using sCr and 24-h proteinuria, both of which correlated well with renal survival [23,24], the ESRD risk was not quantified in these two studies. Our scoring system can quantitatively estimate the ESRD risk in IgA nephropathy patients, using clinical and pathological information collected in routine medical practice.

As shown in Figure 2 and the ROC analysis, our prognostic score works well; even when it is based on randomly selected derivation samples, the score predicted the ESRD risk in the remaining validation sample as accurately as the score derived from the whole dataset. Thus, our estimates among all subjects were fully justified.

Some limitations should also be kept in mind when utilizing the score tables. First, our prognostic score is not able to predict ESRD risk for longer than 7 years (we are conducting a further survey to extend the follow-up period for a longer-term prediction). Second, the endpoint of the present study was focused on ESRD. Although this follow-up study collected sCr values as an outcome in addition to ESRD and deaths, the analytical methods for the change in sCr level over time greatly differ from those for ESRD. We, therefore, will report analyses for the change in sCr values as an outcome after the ongoing extended survey is completed. Third, we did not address the effect of therapy because data on treatment were not obtained at baseline. Further investigations focusing on treatment may be warranted.

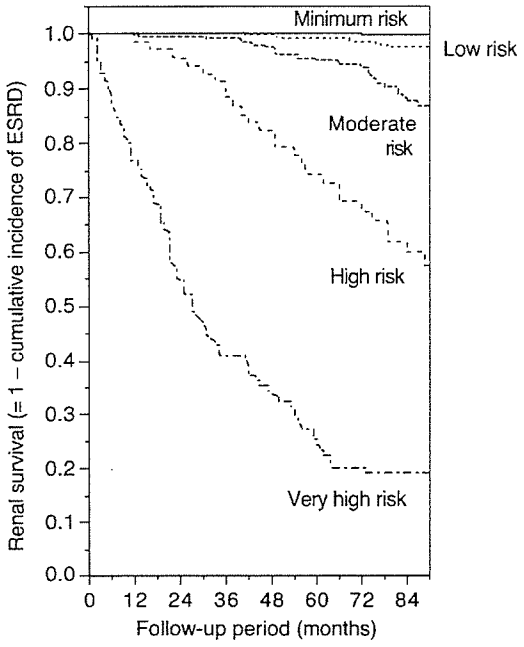

Fig. 2. Renal survival curves by the predicted 7-year risk of ESRD. Patients were categorized into five groups according to the estimated risk: minimum (0.0–0.9%, $n=769$), low (1.0–4.9%, $n=556$), moderate (5.0–19.9%, $n=230$), high (20.0–49.9%, $n=72$) and very high (50.0–100.0%, $n=127$). Numbers of patients at risk were 1754, 1478, 1237, 961 and 817 at 0, 2, 4, 6 and 7 years, respectively.

Another major methodological issue may be related to the limitation of the mail survey as a method to obtain laboratory data and to the quality of some data; about a quarter of the subjects did not have a complete set of data for the scoring system, and we could not check the quality of laboratory data from the participating institutions. The histological grading of biopsy specimens was done in each hospital and the inter-institutional variation in classification may have resulted in the relatively small contribution of histological grade to the prognostic score (Table 3). Because the data at baseline on 24-h urine excretion of protein were not available for two-thirds of the subjects and those on urinary protein to creatinine ratio were not collected, we had to assess proteinuria with a dipstick. The semi-quantified proteinuria was reasonably reproducible; 81.5% of patients were classified into the same or adjacent categories [patients were grouped into (−), (+−), (+), (++) and (+++) of proteinuria] in the two tests 2 years apart (at baseline and at the 1997 survey). The dipstick proteinuria was also rather strongly correlated with the 24-h urinary excretion of protein among patients with the relevant data (Spearman's correlation coefficient, 0.77 at baseline). The misclassification by the dipstick assessment, however, might have attenuated the association between proteinuria and ESRD risk. The use of dipstick did not allow us to estimate the risk for the amount of persistent proteinuria over time as suggested by a previous report [25]. Collecting more detailed laboratory data (e.g. creatinine clearance) will add to the accuracy of risk prediction by the scoring system.

Finally, our scoring system was developed among Japanese patients. It would be applicable to Western populations as well, since renal survival rates by prognostic factors are reasonably comparable between the present subjects and patients in Western countries [5,7,22,26]. To tailor the scoring system for populations other than Japanese, however, it may be warranted to adjust sCr for body weight [21] and racial groups [27] because the sCr level was the most important factor to predict ESRD risk as reflected in the wide range of prognostic scores assigned to this parameter. Additional validation studies may be helpful in optimizing this scoring system for populations of different races.

In summary, the present study found that hypertension, proteinuria, haematuria (particularly mild type), hypoproteinaemia, azotaemia and advanced histological change independently increased the risk of ESRD in IgA nephropathy patients. The ESRD-prediction score based on a multivariate model was sufficiently valid and will serve as a useful tool for IgA nephropathy in clinical practice.

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Conflict of interest statement. None declared.

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