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腎疾患政策研究事業

腎疾患対策検討会報告書に基づく慢性腎臓病（CKD)対策の推進に資する研究

令和4年度～6年度　総合研究報告書

研究代表者　岡田　浩一

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腎疾患対策検討会報告書に基づく慢性腎臓病（CKD)対策の推進に資する研究

研究代表者　岡田 浩一　埼玉医科大学　教授

研究要旨

1　普及啓発：

(1)CKD 普及啓発活動の推進

行政や JKA の連携企業と連携した CKD 普及啓発活動を実施し、CKD 認知度を経年的に調査した結果、漸増傾向が認められた。

(2)普及啓発資材の利活用と新たな開発

既存資材の活用促進と新たな開発を行った。

2　診療連携体制構築：

(1)診療連携体制の構築

JKA と協力し、かかりつけ医（医師会)、腎臓専門医、行政との連携体制を地域の実状に即して構築し、定点観測地域（北海道旭川市、千葉県、岡山県美作市、熊本県熊本市）における進捗状況をモニタリングし、連携に協力するかかりつけ医は漸増していた。また行政と問題点を共有するため各地で CKD 対策意見交換会を開催し、専門医が不足する地域では連携協力医の育成が必要という共通認識を得られた。

(2)紹介基準の普及

かかりつけ医および専門医を対象にアンケート調査を実施した結果、連携を開始すべきと考えるステージはかかりつけ医では G4、専門医では G3b と乖離が進んでいた。そこで「かかりつけ医から腎臓専門医・腎臓専門医療機関への紹介基準」（簡易版）を作成し、その普及を推進した。

(3)診療連携体制の好事例の横展開支援

診療連携体制を効率的に構築・運営している地域（定点観測地域、大阪府、沖縄県南城市）における構築プロセスと運用の実際を CKD 診療連携体制構築プログラムとして構造化し、HP で公開した。

3　診療水準向上：

JSNと協力し、専門医向けのCKD診療ガイドライン、かかりつけ医向けのCKD診療ガイドと患者向けのCKD療養ガイドの改訂出版し、そこに示された標準治療の普及を診療連携体制構築を通して推進した。上述のアンケートや定点観測地域でのモニタリングの結果、かかりつけ医における標準治療の実施率が上昇していた。また治療効果の見える化を通して患者アドヒアランスの維持・改善を目指し、eGFRスロープの変化を簡便に計算できるアプリをHPで公開した。さらに治療効果の見える化を通して患者アドヒアランスの維持・改善を目指し、eGFRスロープの変化を簡便に計算できるアプリをHPで公開した。

4　人材育成：

(1)腎臓病療養指導士制度への支援

各都道府県において腎臓病療養指導士協議会を組織し、制度を支援した。また厚生労働科学研究腎疾患政策研究「慢性腎臓病患者に特有の健康課題に適合した多職種連携による生活・食事指導等の実証研究」と連携し、多職種連携マニュアルの作成と普及に協力した。また CKD 対策支援データベースで公開されている各都道府県における腎臓専門医および腎臓病療養指導士数の年次推移を更新した。腎臓病療養指導士数は漸増傾向を示している。

(2)保健師によるCKD患者への生活指導、受診勧奨を推進するため、保健師を対象としたCKD対策セミナーを開催した。

5　研究開発：

(1) CKD 対策支援データベースの構築

各都道府県の a) 普及・啓発の取り組み、b) 診療連携体制構築の取り組み、c) 腎臓専門医・腎臓病療養指導士数、d) 透析導入患者数を収納した CKD 対策支援データベースを構築・公開した。また eGFR スロープの簡易計算サイトを造設し、その普及に努めた。

(2) 高齢 CKD 患者の透析導入後の生命予後予測式の作成

近年、腎代替療法の選択肢に保存的腎臓療法が加わっており、その選択に際し透析導入後の生命予後は患者と家族にとって重要な情報となる。そこで AMED 研究班「高齢腎不全患者に対する腎代替療

法の開始/見合わせの意思決定プロセスと最適な緩和医療・ケアの構築」と連携して、高齢 CKD 患者の透析導入後の生命予後予測式を作成し、発信した。
(3)CKD 患者数の概算
最新の特定健診データや NDB データなどを用いて、わが国の CKD 患者数を新たに概算し、CKD 患者が 2,000 万人に達することが示された。
(4) CKDに対する集学的治療効果の検証
AMED研究班「糖尿病性腎症、慢性腎臓病の重症化抑制に資する持続的・自立的エビデンス創出システムの構築と健康寿命延伸・医療最適化への貢献」と連携し、J-CKD-DBを用いて、標準治療の集学的効果を実証し、発信した。

以上の取り組みとの因果関係は証明困難だが、日本の新規透析導入患者数は2019年より、また総維持透析患者数は2021年より漸減傾向となっている。

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A．研究目的

本研究では、先行研究である「慢性腎臓病(CKD)に対する全国での普及啓発の推進、地域における診療連携体制構築を介した医療への貢献（令和元年～3年）」を引き継ぎ、厚生労働行政推進調査事業費補助金（腎疾患政策研究事業）「腎疾患対策検討会報告書に基づく対策の進捗管理および新たな対策の提言に資するエビデンス構築」（研究代表：柏原直樹）、日本腎臓学会、日本腎臓病協会のCKD対策部会と連携し、腎疾患対策検討会報告書に基づいたCKD対策の社会実装を推進する。具体的には各都道府県におけるCKD対策を経年的にプロセス・アウトカム評価し、改善点を検討してPDCAサイクルを回し、またCKD診療連携体制の好事例（定点観測地域など）を積極的に横展開することで、全国レベルでのCKD対策を推進することを目的とする。これによりCKD重症化を予防して新規透析導入患者数を減少させ、さらにCKD患者（透析患者及び腎移植患者を含む）のQOLの維持向上を図る。
以下に、同報告書の５本柱に沿った取り組みを示す。

1）普及、啓発
(1) 日本腎臓病協会のCKD対策部会の各ブロック長(分担研究者を兼担)と各都道府県責任者(研究協力者）による腎臓専門医、かかりつけ医、行政と製薬企業と連携した普及啓発活動の推進(令和4年～6年)と有効例の情報公開(令和6年)
(2) 普及啓発資材の利活用の推進と新たな開発
これまでに作成された資材の有効利用を推進し、また必要に応じて新たに作成する(令和4年～6年)。

３）　診療連携体制構築
（１）地域の実情に即したCKD診療連携体制の構築
ブロック長、各都道府県責任者を中心に、かかりつけ医と腎臓専門医・連携協力医との連携体制構築を推進する。その際、定点観測地域（旭川、千葉、岡山、熊本）を中心に、その他のエリアの取り組みの優れた点、問題点・改善点を研究班で検討し、PDCAサイクルを回す(令和4年～6年)。適宜、行政によるCKD診療連携構築モデル事業の申請および糖尿病性腎症重症化予防プログラムとの相乗りを目指す。成果はHP上でデータベースとして年度ごとに公開する(令和4年～6年)。また行政担当者と診療連携体制の重要性に関する意見交換会を開催する。（令和６年）
（２）紹介基準・連携パスの普及
「かかりつけ医から腎臓専門医・腎臓専門医療機関への紹介基準」や各エリアで使用中の紹介基準、連携パスの利活用を推進する(令和4年～6年)。
（３）診療連携体制の好事例の横展開支援
好事例を構造化した CKD 診療連携構築プログラムを作成し、研究班ホームページで公開する(令和６年)。

３）診療水準の向上
日本腎臓学会と連携してガイドライン・ガイドを改訂出版し、標準治療をアップデートする（令和4～6年）。そして病診連携体制を通して、ガイドラインに沿った標準医療の提供を図る(令和4～6年)。

４）人材育成
CKD診療に長けた看護師/保健師、管理栄養士、薬剤師等の人材を育成し、彼らの腎臓病療養指導士の取得を促進し、CKD診療連携体制への参画を推進する(令和4年～6年)。特に専門医不在のエリアにおける腎臓病療養指導士の充足を目指す。また適切な腎代替療法選択の促進のために、腎代替療法専門指導士制度と連携し腎臓病療養指導士のSDMへの関わりを深める(令和4年～6年)。

５）研究開発
CKD 対策支援のために、CKD 患者数の概算（1,329 万人）の見直しを行う(令和 4 年)。また各エリアの取り組み（腎臓専門医や連携協力医、腎臓病療養指導士の所在）や成果（新規透析導入患者数）の年次推移をデータベースとして年度ごとに公開する(令和 4 年～6 年)。
また AMED 研究班と連携し、高齢 CKD 患者の腎代替療法選択時に有用となる透析導入後の生命予後に関する推定式を作成する（令和 4、5 年)。さらに J-CKD-DBEx を用いて、相加・相乗作用のある標準治療の組み合わせを創出し（令和 4 年)、CKD の至適集学的治療として発信し、普及を促進する（令和 5、6 年)。

Ｂ．研究方法

1　普及啓発

(1)CKD 普及啓発活動の推進
各都道府県で行政と連携した CKD 普及啓発活動を実施し、年度末ごとに実施状況をモニタリングする。また日本腎臓病協会と連携協定を結んでいる製薬企業の協力のもと、市民公開講座やマスコミを通してＣＫＤ普及啓発活動を展開する。CKD 認知度は定期的に調査して公開し、年度ごとに更新する。
(2)普及啓発資材の活用と新たな展開
これまでに作成された資材の活用を促進する。またその効果に応じて、新たな開発を行う。

（各ブロック・定点観測地域の取り組みに関しては、令和 4~6 年度の研究班報告書を参照）

2　診療連携体制構築

(1)診療連携体制の構築
各都道府県責任者を中心に、かかりつけ医（医師会)、腎臓専門医・専門医療機関、行政との連携体制の構築を推進する。その連携に腎臓病療養指導士（看護師、薬剤師、栄養士）や保健師、薬局薬剤師等も参画させる。その際、行政や都道府県医師会を通した大規模な連携を構築するトップダウンのアプローチ、腎臓専門医・専門施設とその医療圏におけるかかりつけ医（医師会）との小規模な連携からスタートして横展開するボトムアップのアプローチなど、地域の実情に即して体制構築に取り組む。また行政には、CKD 診療連携構築モデル事業への参画を促す。各エリアの体制構築の進捗状況、腎臓専門医や連携協力医、腎臓病療養指導士の所在情報を調査して公開し、年度ごとに更新する。また CKD 診療・病診連携の実態調査として、2019 年度に引き続き、2024 年度に日本腎臓学会および日本臨床内科医会の協力のもとにアンケート調査を実施する。
行政からの診療連携体制構築への協力を得るため、診療連携体制の重要性と近隣都道府県の好事例を共有する意見交換会を開催する。
(2)紹介基準の普及
「かかりつけ医から腎臓専門医・腎臓専門医療機関への紹介基準」をもとに、簡易版の紹介基準やエリアの実情に即して修正した紹介基準を作成し、診療連携体制構築の一環として普及させる。紹介率（逆紹介率については定点観測地域）の年次推移をモニタリングして公開し、年度ごとに更新する。
(3)診療連携体制の好事例の横展開支援
これまでに旭川市、千葉県、岡山市、熊本市を定点観測地域に選定し、2020年より詳細なモニタリングを開始している。他エリア（大阪府、沖縄県南城市）の優れた取り組みも取り入れ、診療連携体制構築プログラムを作成し、横展開を支援する。この際、各地域の実情に即したa）行政や医師会との連携方法、b）腎臓専門医・専門施設の充足度に応じた対応（連携協力医制度、腎臓病療養指導士・保健師の積極的な登用等）、c）ユニークな紹介基準や連携パスの策定・運用など、いくつかの異なるパターンを選定し、CKD対策支援データベース上で公開する。

（各ブロック・定点観測地域の取り組みに関しては、令和 4~6 年度の研究班報告書を参照）

3　診療水準向上

(1)標準治療の普及
専門医向けのCKD診療ガイドライン2018と患者と家族向けのCKD療養ガイド2018の定期的な改訂に加え、長らく改訂のなかったCKD診療ガイド2012をかかりつけ医への標準治療の普及を目指して改訂することとなり、日本腎臓学会の改訂作業に協力する。

ガイドラインで推奨されている標準診療を、診療連携体制構築の一環として普及促進する。定点観測地域を中心にかかりつけ医におけるガイドラインの普及率と標準治療の実施率の年次推移をモニタリングして公開し、年度ごとに更新する。

(2)eGFRスロープを用いたCKDの重症度評価と治療効果判定の推進

治療効果の見える化を通して患者アドヒアランスの維持・改善を目指し、eGFRスロープの変化を簡便に計算できるアプリをHPで公開する。

（各ブロック・定点観測地域の取り組みに関しては、令和4~6年度の研究班報告書を参照）

4 人材育成

(1) 腎臓病療養指導士の育成

腎臓病療養指導士を積極的に育成し、地域差を是正する。各都道府県において腎臓病療養指導士の協議会（連携の会）を組織し、その支援策について検討する。各エリアにおける腎臓病療養指導士の人数（できれば所属）の年次推移を公開し、年度ごとに更新する。

(2)慢性腎臓病透析予防指導管理料の申請要件であるメディカルスタッフの育成とCKDケアへの参画支援

厚生労働科学研究腎疾患政策研究「慢性腎臓病（CKD）患者に特有の健康課題に適合した多職種連携による生活・食事指導等の実証研究（代表要伸也)」と連携し、「CKDのための多職種連マニュアル」の普及とともにCKD診療に長けたメディカルスタッフの増加を図り、CKD診療連携体制へ積極的に登用する。腎臓専門医が少ない地域では、CKD診療の充実につなげる。

(3)保健師によるCKD患者への生活指導、受診勧奨を推進するため、保健師を対象としたCKD対策セミナーを実施する。

（各ブロックの取り組みに関しては、令和4~6年度の研究班報告書を参照）

5 研究開発

(1) CKD対策支援データベースの構築・公開と運営

各都道府県の a）普及・啓発の取り組みと認知度(visual abstract)、b）診療連携体制構築の取り組み(visual abstract)、c）腎臓専門医・連携協力医の所属、d）腎臓病療養指導士数、e）新規透析導入患者数（人口当たり・年齢調整）の年次推移を収納したCKD対策支援データベースを構築・公開し、データ利活用（閲覧数）の向上を目指しつつ経年的にデータを更新する。

またタンパク尿を伴わないCKD患者の重症度・予後判定や治療効果の見える化のために、新たに複数の血清クレアチニン値を入力すると eGFR スロープの値が自動計算され、また何らかの介入を行った際のその前後の eGFR スロープの変化が簡便に求められる機能を追加する。

(2)高齢 CKD 患者の透析導入後の予後規定因子の同定

日本の高齢ＣＫＤ患者の透析導入後の生命予後に関して、中長期生命予後は諸外国に比較して良好だが、短期生命予後はほぼ同等であり、中長期の生存が期待できない患者が導入されている可能性が示唆される。また近年は末期腎不全患者に対する腎代替療法の選択肢として、血液透析、腹膜透析、腎移植に保存的腎保護療法が加わっており、高齢CKD患者には短期生命予後が血液透析と保存的腎保護療法とでほぼ同等な患者群が報告されている。腎代替療法の選択に際し、血液透析導入後の短期生命予後は患者と家族にとって重要な情報となる。そこでAMED研究班「高齢腎不全患者に対する腎代替療法の開始/見合わせの意思決定プロセスと最適な緩和医療・ケアの構築」と連携して高齢CKD患者の透析導入後の短期生命予後予測式を作成する。

(3)CKD患者数推定

①CKD患者数の実態調査:

わが国のCKD有病者数を調査する方法として、特定健診データ、各地のコホート研究、NDB データなど、どのデータを用いるのが適切か検討した。CKD 有病割合の推定について、集団の特性によって推定値が影響を受けるため、就労世代の健保データ、高齢世代を中心とした自治体国保データの両者の分析を行う。また、健診受診者、医療機関受診者の結果を一般集団に外挿する際にはサンプリングバイアスの影響を考慮する必要があるため健診受診（医療機関受診）確率を推定し、受診確率によって重みづけしたCKD有病割合推定を行う。

②CKD患者数に影響を与える因子の解明:

わが国のCKD患者数は、高齢化や糖尿病など生活習慣病の影響で増加していることが予想される。しかしながら、それらの要因の影響は地域によって差があることが予想される。わが国のCKD対策の均霑化のためにも、CKD 患者数に影響を与える因子を解明することは重要である。そこで、大阪府内での生活習慣病罹患率とCKD罹患率の関連を

検討することとした。また、上記の CKD 患者数の実態調査において、CKD 患者数に影響を与える因子を解明する方法についても検討した。個人レベルでの CKD リスク因子に関する検討も行う。健診で取得される古典的なリスク因子に加えて社会経済因子等の検討も行う。

(4) CKDに対する集学的治療効果の検証
AMED 研究班「糖尿病性腎症、慢性腎臓病の重症化抑制に資する持続的・自立的エビデンス創出システムの構築と健康寿命延伸・医療最適化への貢献」と連携し、J-CKD-DBEx を用いて、CKD に対する集学的治療（標準治療の組み合わせ）の有効性を検証する。

本研究班の連携状況と活動の全体像を以下にしめす。

（倫理面への配慮）
アンケート調査やデータベース解析等の個人情報に関わり得る取り組みに際しては、分担研究者の所属施設の倫理委員会等で適切な審査・承認を受けた上で実施する。

C. 研究結果
1　普及啓発
(1) 日本腎臓病協会と連携した普及啓発活動
　各都道府県および定点観測地（北海道旭川市、千葉県、岡山県美作市、熊本県熊本市）において、日本腎臓病協会 JCKDI 分科会ブロック長・定点観測地責任者（研究分担者）と地区リーダー（研究協力者）のリーダーシップのもと、行政と協力しつつ、様々な普及啓発の試みがなされた。本研究班および日本腎臓病協会と連携し、全国で CKD 普及啓発のイベントが 2022 年度には 135 回、2023 年度には 148 回、2024 年度に 140 回開催され、コロナ禍以前のレベル（2019 年 128 回）を上回ることができた。(参照：厚生労働行政推進調査事業費補助金腎疾患政策研究事業ホームページ「全国の取り組み・年次推移　ー各都道府県の腎臓病の「いま」が見えるー」（https://ckd-research.jp/promotion/#sec02））

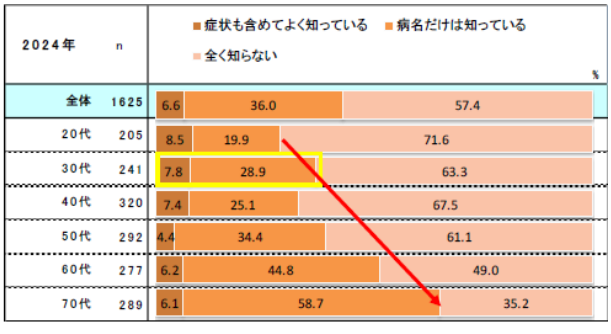
（例：埼玉県のデータ）
　さらに日本腎臓病協会と連携協定を締結した製薬企業の協力のもと、新たなチャネルを通した普及啓発活動を行った。

(2) 普及啓発資材の利活用の推進と新たな開発

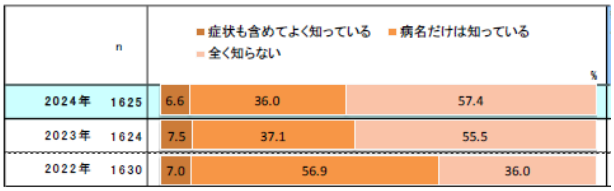
日本腎臓病協会および CKD 対策研究班がこれまでに作成した資材の利活用を促進するため、研究班ホームページ(https://ckd-research.jp/)で公開した。また本研究班でも新たに未病、有リスク者への啓発資材を作成し、ホームページでダウンロード可能なファイルとして公開した。

啓発動画を収録した DVD を作成し、世界腎臓デーに向けて関連病院で放映していただいた。

これらの取り組みと並行して一般市民の CKD 認知度調査を継続して実施し、年齢層が上がるにつれて認知度が高くなる傾向が認められた。



また 2019 年から 2022 年まで漸増傾向であったが、それ以降は 2023 年、2024 年と漸減となっていた。

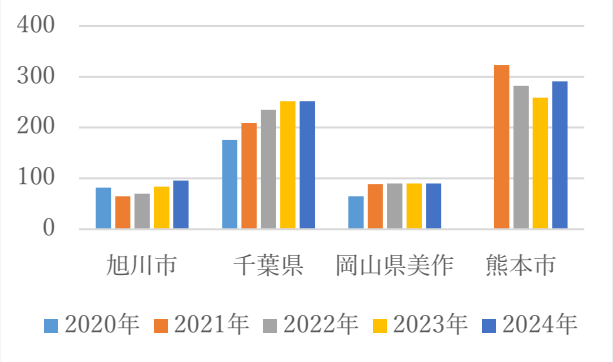


（各ブロック・定点観測地域の取り組みに関しては、令和 4~6 年度の研究班報告書を参照）

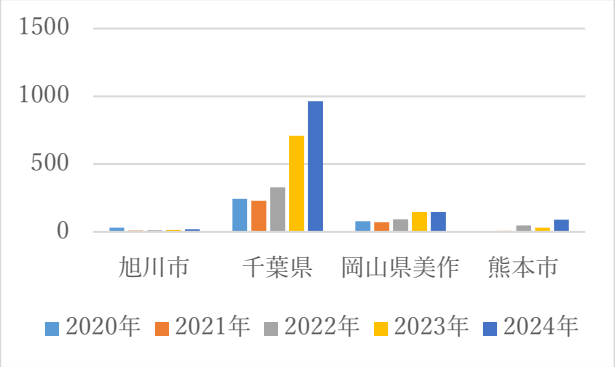
2　診療連携体制構築

(1) 地域の実情に即した CKD 診療連携体制の構築

各都道府県および定点観測地（北海道旭川市、千葉県、岡山県美作市、熊本県熊本市）において、日本腎臓病協会 JCKDI 分科会ブロック長・定点観測地責任者（研究分担者）と地区リーダー（研究協力者）のリーダーシップのもと、行政および医師会と協力しつつ、様々な診療連携体制構築の試みがなされ、横展開用情報として研究班ホームページで公開した。（厚生労働行政推進調査事業費補助金腎疾患政策研究事業ホームページ「全国の取り組み・年次推移　ー各都道府県の腎臓病の「いま」が見えるー」（https://ckd-research.jp/promotion/#sec02））　連携制度の構築とその効果を検証するための定点観測地域では、連携制度数は変動があるものの、連携に参加するかかりつけ医数は増加もしくは高め安定で推移している。

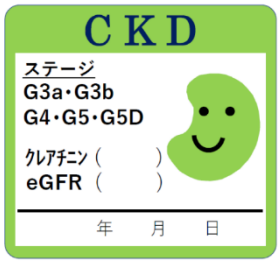


定点観察地域における連携かかりつけ医数の推移



定点観察地域における連携管理下の患者数の推移

薬局薬剤師による CKD 診療への連携を通し、CKD 患者の行動変容への協力とともに、腎機能に応じた処方の確認、腎毒性薬剤が投与されていないかの確認を促進するため、おくすり手帳に貼付する CKD シールを作成して、研究分担者を通して配布した。



各地域における診療連携体制の構築に行政の理解と協力を得るために、本研究班の研究分担者と協力者（日本腎臓病協会 JCKDI ブロック長と都道府県代表者）と行政担当者との意見交換会をブロック単位で開催した。

・北・南北海道ブロック　令和 6 年 11 月 28 日
・東北ブロック　令和 6 年 11 月 6 日
時間：15：00～17：00
場所：TKP ガーデンシティ仙台　カンファレンスルーム 21E
・北関東ブロック　令和 6 年 12 月 23 日
時間：17:00-18:00
Web 開催
・南関東・東京ブロック　令和 6 年 12 月 15 日
時間：10：00~12：00
場所：ステーションカンファレンス東京
・北陸ブロック　令和 6 年 11 月 24 日
時間：13：00～15：00
場所：大宮ソニックシティ 7 階　701 会議室（ハイブリッド開催）
・東海ブロック　令和 6 年 11 月 27 日
時間：18:00～20:00
場所:TKP ガーデンシティ PREMIUM 名古屋ルーセントタワー
・近畿ブロック　令和 6 年 11 月 10 日
時間：13:00～15:0

場所：TKP ガーデンシティ PREMIUM 大阪駅前
・中国ブロック　令和 6 年 10 月 11 日
時間：15:00~17:00
場所：岡山コンベンションセンター301 号室
・四国ブロック　令和 6 年 11 月 1 日
時間：16:00~17:30
Web 開催

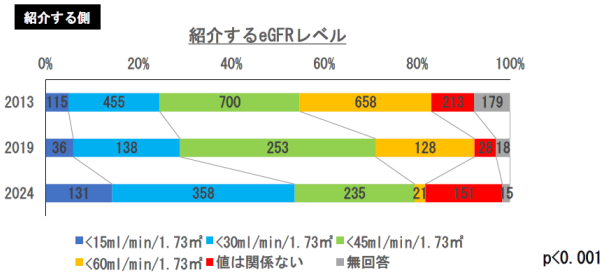
（四国ブロック意見交換会　令和 6 年１１月１日開催）
・九州・沖縄ブロック　令和 6 年 12 月 13 日　時間：16:00～18:00
場所：　TKP ガーデンシティ博多駅前

(2)紹介基準の普及
日本腎臓学会が日本医師会の協力のもとで作成したかかりつけ医から腎臓専門医への紹介基準が作成されている。(エビデンスに基づく CKD 診療ガイドライン 2023(東京医学社))

原疾患		蛋白尿区分		A1	A2	A3
糖尿病		尿アルブミン定量(mg/日) 尿アルブミン/Cr比(mg/gCr)		正常	微量アルブミン尿	顕性アルブミン尿
				30未満	30～299	300以上
高血圧 腎炎 多発性嚢胞腎 その他		尿蛋白定量(g/日) 尿蛋白/Cr比(g/gCr)		正常 (－)	軽度蛋白尿 (±)	高度蛋白尿 (＋～)
				0.15未満	0.15～0.49	0.50以上
GFR区分 (mL/分/ 1.73 m^2)	G1	正常または高値	≧90		血尿＋なら紹介，蛋白尿のみならば生活指導・診療継続	紹介
	G2	正常または軽度低下	60～89		血尿＋なら紹介，蛋白尿のみならば生活指導・診療継続	紹介
	G3a	軽度～中等度低下	45～59	40歳未満は紹介，40歳以上は生活指導・診療継続	紹介	紹介
	G3b	中等度～高度低下	30～44	紹介	紹介	紹介
	G4	高度低下	15～29	紹介	紹介	紹介
	G5	末期腎不全	＜15	紹介	紹介	紹介

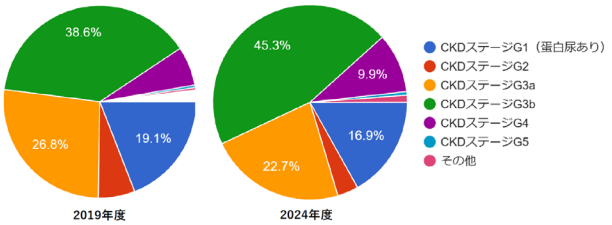
上記以外に，3カ月以内に30%以上の腎機能の悪化を認める場合は速やかに紹介．
上記基準ならびに地域の状況等を考慮し，かかりつけ医が紹介を判断し，かかりつけ医と腎臓専門医・専門医療機関で逆紹介や併診等の受診形態を検討する．
かかりつけ医から腎臓専門医への紹介基準

近年、糖尿病関連腎臓病(DKD)や CKD に対する進行抑制効果が示された集学的治療や SGLT2 阻害薬の末期腎不全への進展抑制に関して、CKD ステージ G4（GFR<30）以降では有意な効果が認められないとする報告がなされている。(Clin J Am Soc Nephrol 2020;15:1705-1714, J Diabetes Investig 2021;12:207-216, J Am Soc Nephrol 2021;32:2352-2361, Clin Kidney J 2023;16:1187)
日本臨床内科医会が日本腎臓学会との合同企画として実施したかかりつけ医を対象とする CKD 診療実態アンケート調査の結果では、2019 年度に腎臓専門医への紹介が最も多い CKD ステージは G3b、次いで G4 であった。(J Clin Med 2022;11:4779)。しかし 2024 年度の調査では、G4 ステージが増加して最も多くなり、また G5 ステージも増加しており、より進行したレベルまでかかりつけ医が単独で診療する傾向が認められた。



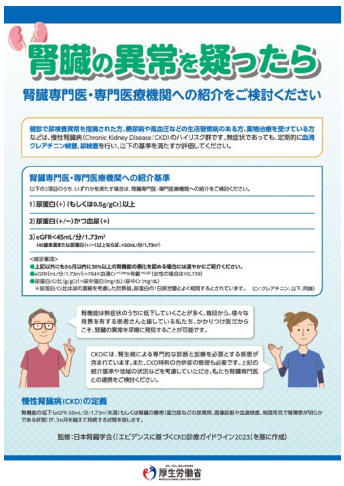
かかりつけ医が腎臓専門医に紹介すべきと考える CKD ステージの推移（日本臨床内科医会）

一方、日本腎臓学会が実施した腎臓専門医アンケート調査の結果、かかりつけ医との連携を開始すべきと考える CKD ステージは、2019 年度では最多が G3b(38.6%)、ついで G3a(26.8%)であった。2024 年度では G3b(45.3%)、ついで G3a(22.7%)となっており、G3b ステージで連携を開始すべきという意見が半数近くを占めている。



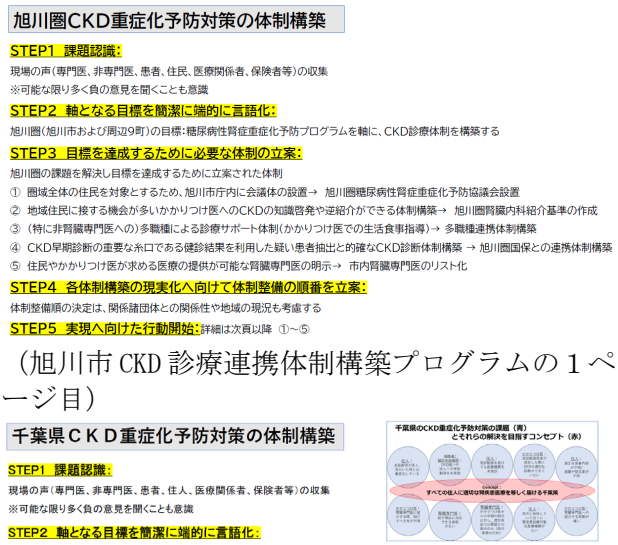
腎臓専門医がかかりつけ医と連携を開始すべきと考える CKD ステージの推移（日本腎臓学会）

以上のように、かかりつけ医と腎臓専門医間に紹介・連携すべきと考える CKD 患者ステージに格差があり、集学的治療などの標準治療の有効性を最大化するためには、G3b（eGFR30～45）での紹介をさらに推進すべきと考えられた。そこで厚生労働省健康・生活衛生局難病対策課・がん疾病対策課と協力し、かかりつけ医向けの簡便な紹介基準のパンフレット「腎臓の異常を疑ったら」を作成し、その中で eGFR≦45 からのかかりつけ医から腎臓専門医への紹介を推奨した。本パンフレットは本研究班班長の岡田浩一が企画・監修した日本医師会雑誌特集号「病診連携と多職種で取り組む日本の CKD 対策」(2024 年 7 月号)とともに全国の医師会員に向けて配布した。

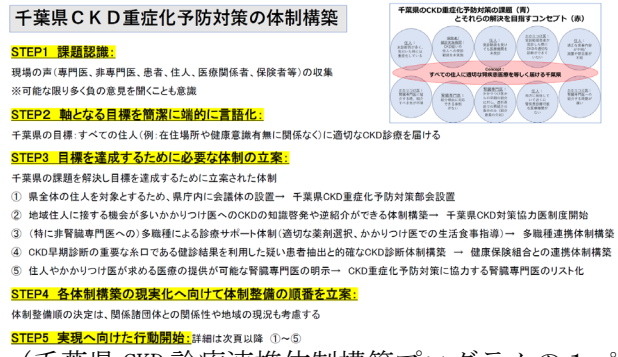


(3) 診療連携体制の好事例の横展開支援

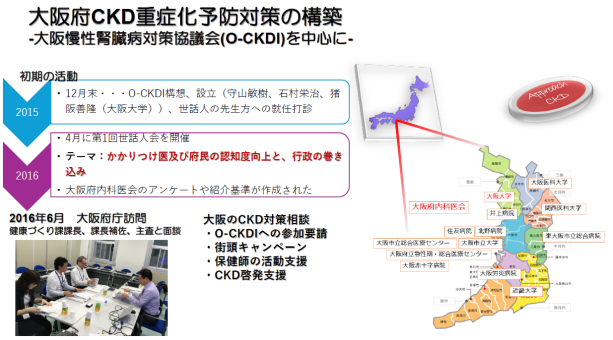
これから診療連携体制の構築を目指す地域を支援するために、定点観測地域および他の好事例エリア（北海道旭川市、千葉県、大阪府、岡山県美作市、熊本県熊本市、沖縄県南城市）に関して、それぞれの取り組みを構造化した診療連携体制構築プログラムを作成し、HP に公開した。（https://ckd-research.jp/regional/ ）



（旭川市 CKD 診療連携体制構築プログラムの１ページ目）

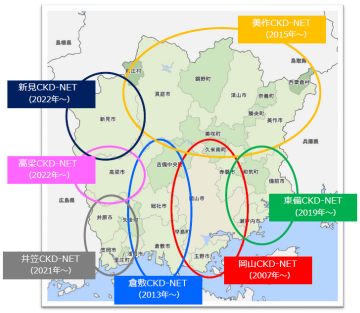


（千葉県 CKD 診療連携体制構築プログラムの１ページ目）



（大阪府 CKD 診療連携体制構築プログラムの１ページ目）

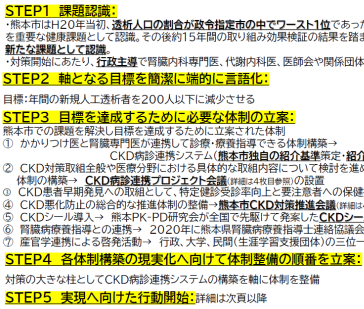
岡山県におけるCKD診療連携



岡山県においては、2007年に岡山大学主導で岡山CKDネットワークが立ち上がり、以後各地域でCKD診療連携システムが構築され、2022年には岡山県全域でCKD診療連携のシステムが整備されるに至っている。運営方法や活動内容などについては、各ネットワークで独自のやり方を行っている。

岡山県北部地域では2015年に美作CKDネットワークが立ち上がり、県北のかなり広い範囲にわたる診療連携を担っている。また、同エリア内には6つの医師会が存在しているが、ネットワークの活動に積極的に協力いただいている。

（岡山県美作市 CKD 診療連携体制構築プログラムの１ページ目）



（熊本市 CKD 診療連携体制構築プログラムの１ページ目）

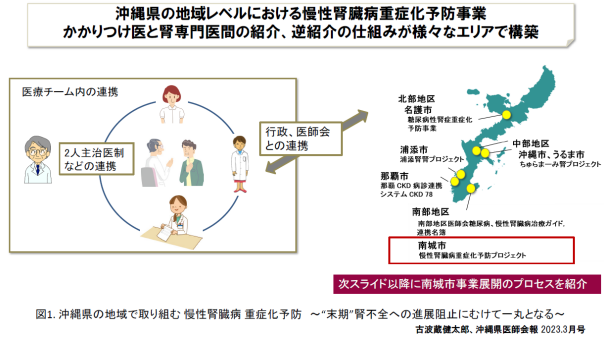


図1. 沖縄県の地域で取り組む 慢性腎臓病 重症化予防 ～"末期"腎不全への進展阻止にむけて一丸となる～
古波蔵健太郎、沖縄県医師会報 2023.3月号

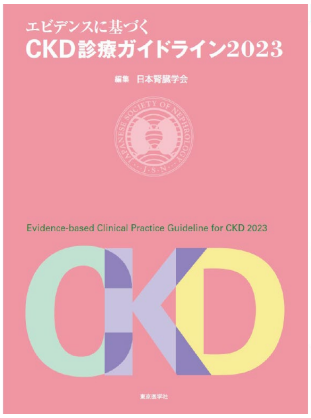
（沖縄県南城市 CKD 診療連携体制構築プログラムの１ページ目）

（各ブロック・定点観測地域の取り組みに関しては、令和 4~6 年度の研究班報告書を参照）

3　診療水準向上

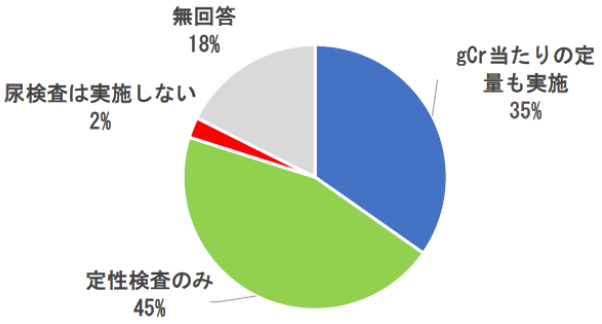
各都道府県および定点観測地（北海道旭川市、千葉県、岡山県美作市、熊本県熊本市）において、日本腎臓病協会 JCKDI 分科会ブロック長・定点観測地責任者（研究分担者）と地区リーダー（研究協力者）のリーダーシップのもと、行政および医師会と協力しつつ、様々な診療水準の向上の試みがなされた。

最新のエビデンスに則った CKD の標準治療の普及のため、日本腎臓学会と連携して腎臓専門医向けの CKD 診療ガイドライン 2023 と患者・家族向けの CKD 療養ガイド 2024 を 5~6 年ぶりに改訂出版した。

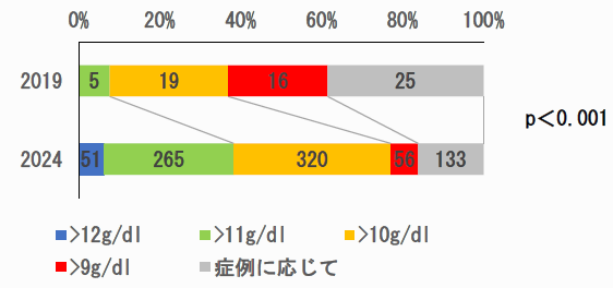


またかかりつけ医向けの CKD 診療ガイドは、CKD 診療ガイドライン 2018 が専門医およびかかりつけ医に向けて改訂出版されたことから、CKD 診療ガイド 2012 以降改訂がなされていなかった。しかし大阪府での実態調査で CKD 診療ガイド 2012 に比較し、CKD 診療ガイドライン 2018 がかかりつけ医に十分普及していないことが明らかとなり（猪阪義隆他、大阪府内科医会会誌 2021;30:70）、12 年ぶりに CKD 診療ガイド 2024 として 12 年ぶりに改訂出版してかかりつけ医への普及を推進した。

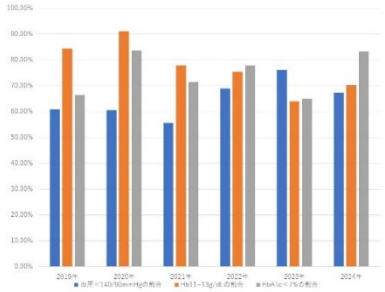
前述の日本臨床内科医会によるかかりつけ医への CKD 診療実態に関するアンケート調査では、CKD 患者に対して検尿を行うと回答したかかりつけ医が 80%に達しており（2024 年度）、重症度分類が適正に行える情報収取がなされていた。



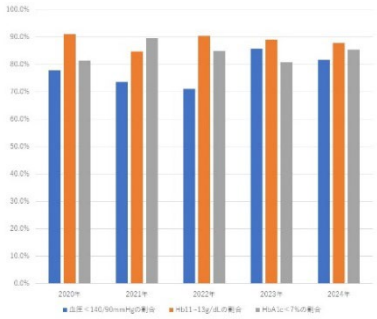
また経口 HIF-PH 阻害薬が保険収載となり、かかりつけ医でも腎性貧血管理に直接関与する機会が増えている現状での目標ヘモグロビン値に関しては、2019 年度に比較して 2024 年度では標準治療として推奨されている>10g/dL と回答したかかりつけ医が 40%から 76%へと著明に増加しており、CKD 診療水準の向上が示唆された。



定点観測地域では、連携制度内で管理された CKD 患者における標準治療の達成率は漸増傾向を示すか、高い状態が維持される傾向が認められたが、遵守率が変動する地域も認められた。



連携体制の下での標準治療の達成率（千葉県）



連携体制の下での標準治療の達成率（岡山県美作）

1）eGFRスロープを用いたCKDの重症度評価と治療効果判定の推進

蛋白尿を伴わない CKD（腎硬化症など）では CKD 重症度分類による重症度判定が困難で、また治療介入効果の見える化（蛋白尿の減少など）が難しいために患者のアドヒアランスの低下を招くことがある。そこで CKD 治療効果のハードエンドポイント（血清クレアチニン値の倍加など）に代わるサロゲートエンドポイントとして日本人 CKD 患者の治療効果判定に有用とされる eGFR スロープの変化（傾きの差分）を簡便に計算できる機能を本研究班ＨＰに装備した。（https://ckd-research.jp/admin/calculate_egfr/ ）差分が 0.5ml/分/1.73m^2/年以上ある場合、有意な腎イベント抑制（CKD 進展抑制）効果と判定できる。

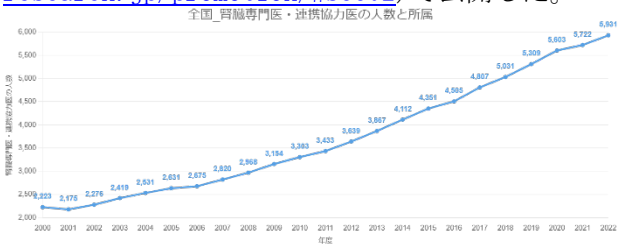
eGFR スロープ簡易計算アプリの出力画面

（各ブロック・定点観測地域の取り組みに関しては、令和 4~6 年度の研究班報告書を参照）

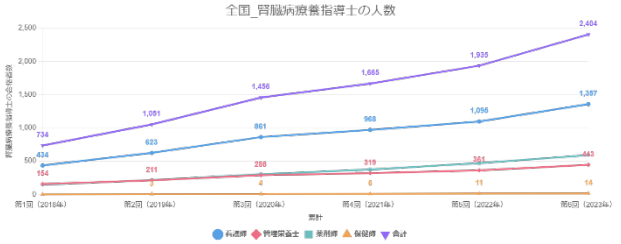
4　人材育成

日本腎臓学会および日本腎臓病協会と連携し、腎臓病療養指導士の育成と資格取得を推進し、2025 年 4 月 1 日現在の腎臓病療養指導士資格保有者は 2,635 名（前年比 241 名増）となった。

各都道府県における腎臓専門医および腎臓病療養指導士数は順調に増加傾向を示し、その年次推移を本研究班ホームページ CKD 対策支援データベース（https://ckd-research.jp/promotion/#sec02）で公開した。



（腎臓専門医数（全国）の年次推移）

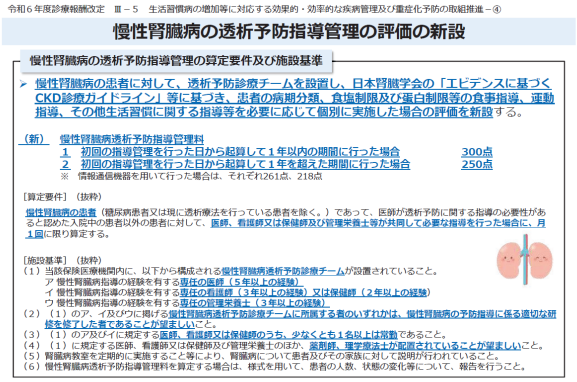


（腎臓病療養指導士数（全国）の年次推移）

また厚生労働科学研究費補助金（腎疾患政策研究事業）「慢性腎臓病(CKD)患者に特有の健康課題に適合した多職種連携による生活・食事指導等の実証研究」（班長要伸也）と連携し、多職種による CKD 対策に関するガイドを作成し、成果物を日本腎臓病協会 J-CKDI 地区代表（本研究班の研究分担者・研究協力者）を通して CKD 診療に関わる多職種へ配布した。

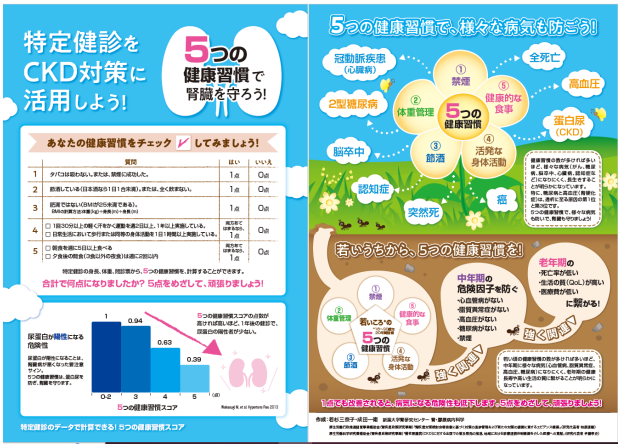
また多職種連携の多施設共同研究（全国の 24 施設、3015 名が参加）により、多職種介入が CKD ステージ G3～G5 において腎機能悪化を抑制することが明らかとなった（Abe M, Kaname S, Clin Exp Nephrol, 2023, Abe M, Kaname S, Front Endocrinol 2023, Abe M, Kaname S, Kidney Res Clin Pract 2025）。さらに追加解析により、ステ

ージ G3bA1 を含むオレンジゾーンの CKD 患者にも多職種介入が有効であること、介入前の腎機能低下が大きい群で効果が見られること、介入前の蛋白尿の程度によらず効果が見られることを明らかにした。そのエビデンスを踏まえて令和６年６月より「慢性腎臓病透析予防指導管理料」が新設され、腎臓病療養指導士等の関わる CKD ケアの更なる普及が期待される。



メディカルスタッフによる CKD 診療サポートの有効性および診療報酬の新設を踏まえ、保健師による有リスク者への、CKD 患者・有リスク者への保健指導・受診勧奨を推進するために、保健師を対象とした CKD 対策セミナーを企画し、保健師介入の重要性とその好事例を紹介した。（2023 年 12 月 16 日に WEB 開催、当日視聴者 1000 名以上、後日オンデマンド視聴者 700 名以上）

また保健指導・受診勧奨に利活用できるツールを本研究班ホームページ（https://ckd-research.jp/）に公開した。



（各ブロックの取り組みに関しては、令和 4~6 年度の研究班報告書を参照）

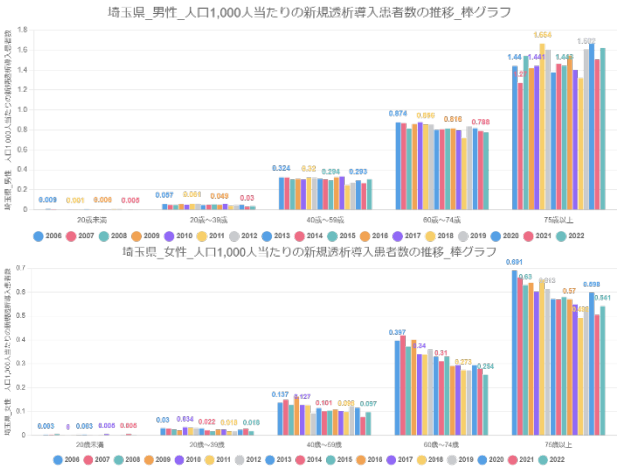
5　研究開発

(1)CKD 対策支援データベースの運営

R４年度に開設した研究班ホームページ（https://ckd-research.jp/）中に CKD 対策支援データベース「全国の取り組み・年次推移　ー各都道府県の腎臓病の「いま」が見えるー」（https://ckd-research.jp/promotion/#sec02）を造設した。

全国の取り組み・年次推移　ー各都道府県の腎臓病の「いま」が見えるー

その中で、各都道府県の CKD 対策の進捗状況（普及啓発の取り組み、CKD 診療連携の取り組み、人口 1000 人当たりの新規透析導入患者数（男女別、年齢階級別）の年次推移、腎臓専門医数、腎臓病療養指導士数の年次推移）を見える化し、研究者のみならず行政関係者から一般市民まで広く活用できるように公開した。透析導入率は都道府県により異なっていたが、全国レベルでは、新規透析導入患者数は 2019 年より 2023 年にかけて順調に減少傾向となっている。



（例：埼玉県のデータ）

保存的腎臓療法の指針

本研究班ホームページは 2023 年２月に公開し、順調にユーザー数（特に新規ユーザー数）を増やしており、有効に利活用されていることが想定される。

【2023年度】

	1Q	2Q	3Q	4Q
ページビュー(表示回数)	7970	11417	25502	18990
ユーザー(訪問者数)	967	1639	6916	4221
新規ユーザー(新規訪問者数)	780	1408	6129	3912
平均エンゲージメント時間(滞在時間)	4:49	2:21	1:33	2:11

【2024年度】

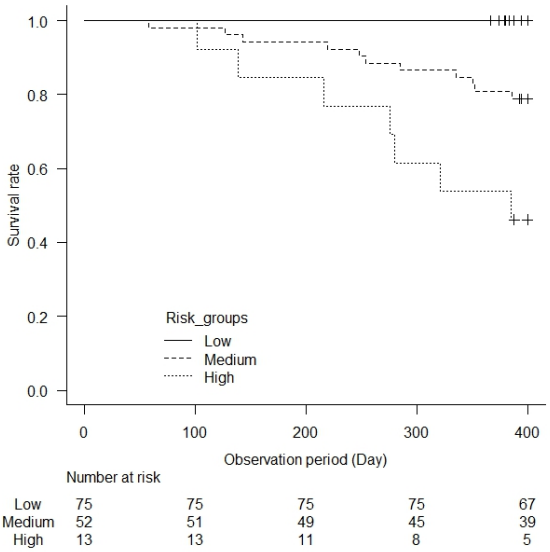
	1Q	2Q
ページビュー(表示回数)	11473	14029
ユーザー(訪問者数)	2874	4042
新規ユーザー(新規訪問者数)	2504	3625
平均エンゲージメント時間(滞在時間)	1:35	1:31

(2023~2024 年度 4 半期ごとの HP 閲覧者数)

(2) 高齢 CKD 患者の透析導入後の予後規定因子の同定

AMED 研究班「高齢腎不全患者に対する腎代替療法の開始/見合わせの意思決定プロセスと最適な緩和医療・ケアの構築」が作成した日本初の保存的腎臓療法のガイドラインの普及を通して、透析療法と移植以外の腎代替療法の選択肢を国民に向けて周知をはかった。

保存的腎臓療法を含む腎代替療法の選択に際し、患者と家族に提示されるべき、血液透析を選択した場合の短期生命予後について、そのリスクを算出するための日本人高齢 CKD 患者用の予後推定式を AMED 研究班と連携して作成した。後ろ向きコホート研究によって透析導入直前の９つのリスク因子が独立して１年以内の短期死亡に関与し、各因子に重みづけをして求めたリスクスコアと死亡リスクが有意に相関することを見出し、前向きコホート研究によって有用性を実証した。



(Okada H, et al. PLoS One 2024;19:e0302101)（資料１）

(3) CKD 患者数の概算

2005 年の CKD 患者数の調査では特定健診データ、各地のコホート研究データが用いられている。本調査においても、上記データを用いて、年次的な推移などを調査することも検討したが、地域に偏りがあることや、会社の健診データを使用することは個人情報保護の観点から利用が難しいこともあり、NDB データを用いた解析を行うこととした。NDB データを用いた解析では全患者データに

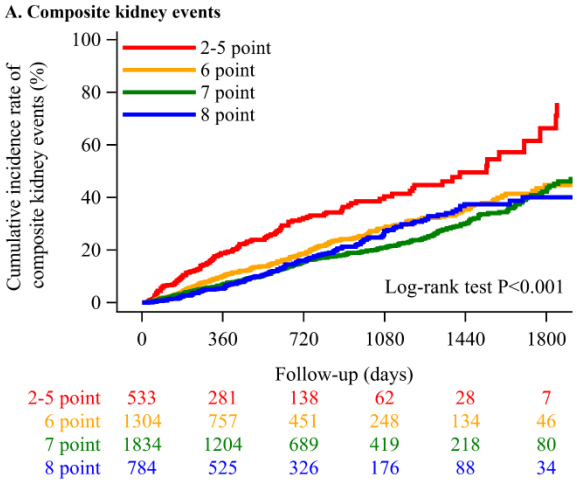
よる解析と部分抽出データによる解析を並行して行うこととした。また、全国規模国保組合、全国協会けんぽ、自治体国保データでの CKD 有病割合推定アルゴリズムを設計した。

65 歳以上の高齢者については、DeSC データを分析し、自治体国保に所属する 65 歳～90 歳高齢者 298 万人を対象とした。年齢、性別、本人・被扶養者、過去健診受診状況で重み計算を行い、各年齢別に CKD の割合を求めた。65 歳から 69 歳、70 歳から 74 歳、75 歳から 79 歳、80 歳から 84 歳、85 歳から 89 歳における CKD の割合はそれぞれ 9.6%, 13.43%, 25.47%, 36.21%, 49.41%であった。本研究では 90 歳以上の CKD の割合は測定していない。2025 年 1 月の人口推計概算値はそれぞれの年代で、724 万人、805 万人、803 万人、612 万人、396 万人となり、CKD 患者数はそれぞれ 69.5 万人、108.1 万人、204,5 万人、221.6 万人、195.2 万人となる。90 歳以上の高齢者における CKD 患者の割合を 50%とすると、65 歳以上の高齢者の CKD 患者数は 940 万人と推定される。30 歳から 64 歳については、全国協会けんぽデータを分析した。年齢、性別、本人・被扶養者、過去健診受診状況、保険料率で重み計算を行った。CKD 患者の割合は 17.08%であり、2025 年 1 月の人口推計概算値は 20 歳以上 64 歳以下が 6815 万人であり、20 歳から 64 歳における CKD 患者数は 1164 万人と推定される。以上からわが国における CKD 患者数は 2104 万人と推定される。なお、重みづけの計算によって推定値が変わる可能性があり、現在の推定値は最終的なものではない。これらの推計からわが国の CKD 患者数は 2000 万人以上も存在する可能性があり、今後、NDB データなどのさらなる解析が必要となる。(CKD ガイド 2024)

また同じ都道府県内でも市町村により異なることが予測される。地域の実情に応じて、CKD 対策に取り組むために、地域における CKD 患者数を知ることができれば役立つことが期待される。そこで特定健康診査データが掲載されているレセプト情報・特定健診等情報データベース（National Database：NDB）のオープンデータを用いて，新潟県の健診受診者（40～74 歳）の性年齢階級別 CKD 有病率を算出した。その際、健診受診者の CKD 有病率が，地域住民の CKD 有病率と同じという仮定を置き，新潟県の性年齢階級別人口から，新潟県民 40～74 歳における CKD 患者数を求めた。新潟県民 40～74 歳のうち，2019 年の特定健診および人口データから計算した CKD 患者数は，男女合わせて 153,175 人（男性 87,738 人，女性 65,437 人）と推計された。この数字は，新潟県民 40～74 歳人口の 14%に相当（男女別では，男性 16%，女性 12%）し，新潟県民 40～74 歳のおよそ 7 人に 1 人（男女別では，40～74 歳男性の 6 人に 1 人，40～74 歳女性の 8 人に 1 人）が CKD と推計された。各自治体などが保有する地域の健康診査データを用いて計算を行えば，40～74 歳に限らず，他の年代での CKD 患者数も同様に推計可能である。健診データを活用することで，毎年，地域における CKD 患者数の最新情報を簡便に地域住民に届けることができると考えられる。(若杉三奈子、他. 日腎会誌 2023;65:485)

(4)集学的治療効果

日本腎臓学会が CKD 診療ガイド・CKD 診療ガイドラインを通して発信してきた標準治療の目標達成数と CKD 進展抑制との関連性を J-CKD-DBEx を用いて検討した結果、推奨された目標の達成数が 6 つ以上の CKD 患者群は、5 つ以下の CKD 患者群に比較して、有意に CKD 進展が抑制されていた。本成果は国内外の学会で報告の上で、論文化した。



(Nyma Z, et al. Sci Report 2024;14:11481)
（資料２）

(5) 透析導入患者の質的変化

①BMI 経年変化

男性透析導入患者では、年齢調整した肥満者の割合が 2006 年調査で 18.9%と、一般住民男性（28.1%）よりも低かった。2019 年調査でも男性透析導入患者では 29.5%と、一般住民男性（32.6%）よりも肥満者の割合は低かったが、その増加率は男性透析導入患者が上回っていた（年平均変化率は、男性透析導入患者で 3.36［95% 信頼区間、2.70～4.09］、一般住民男性は 0.87［95% 信頼区間、0.26～1.42］）。

女性透析導入患者では、年齢調整した肥満者の割合が 2006 年調査で 15.7%と、一般住民女性（20.6%）よりも低かったが、2019 年には女性透析導入患者で 24.9%と、一般住民女性（20.6%）よりも高くなっていた。その増加率は、女性透析導入患者では有意な増加率を認めたのに対し（年平均変化率 2.86［95% 信頼区間、1.65～4.19］）、一般住民女性では有意な増加を認めなかった（年平均増加率 0.01［95% 信頼区間、-0.55～0.57］）。

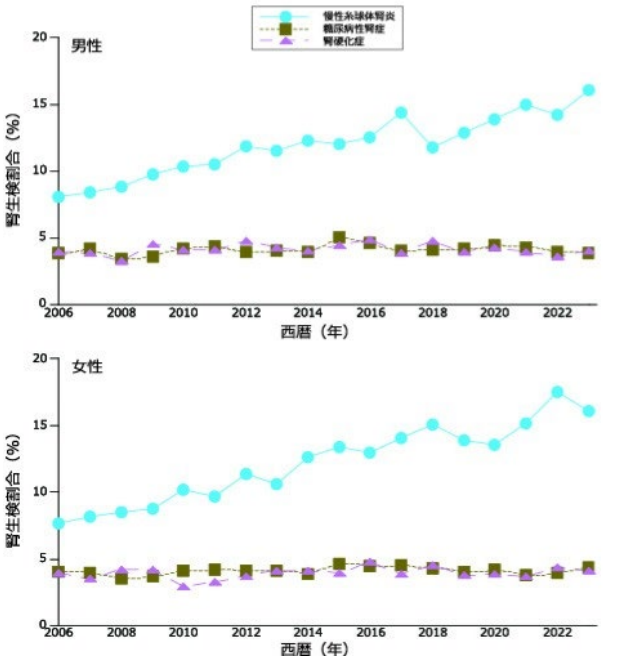
年齢階級別にみると、男女とも 20 代を除く全ての年代で透析導入患者では肥満者の割合が有意に増加していた。2006 年調査で最も肥満者の割合が高かった年代は、男性透析導入患者は 30 代（肥満者の割合は 35.1%）、女性透析導入患者は 40 代（23.0%）であったが、2019 年調査では、男女とも 40 代の透析導入患者で肥満者の割合が最も高かった（男性 47.4%、女性 33.8%）。透析導入患者で肥満者の割合増加が最も急激であった年代は、男性は 60 代（年平均変化率　6.10［95% 信頼区間、5.43～6.91］）、女性は 50 代であった（年平均変化率　3.67［95% 信頼区間、2.59～4.79］）。これほど急激な肥満者の割合増加は一般住民では認められず、その結果、男女とも研究期間の最後（2019 年）の時点では、60 歳未満の全ての年代で透析導入患者の肥満者の割合が一般住民よりも上回っていた。

一方、透析導入患者では年齢調整した低体重の割合が男女とも有意に減少していた（年平均変化率　男性　-2.32［95% 信頼区間、-3.58～-1.13］、女性　-1.59［95% 信頼区間、-3.09～-0.04］）が、なおもその割合は一般住民よりも遥かに高く、特に高齢の透析導入患者で顕著であった。2019 年調査では、年齢調整した低体重の割合は、透析導入患者では男性 10.9%、女性 21.0%と、一般住民（男性 4.0%、女性 9.8%）の 2 倍以上であった。年代別では、低体重の割合が最も高かったのは男女とも 80 代以上で、透析導入患者では男性 21.9%、女性 32.0%と、一般住民（男性 5.3%、女性 12.1%）よりも遥かに高かった（2019 年調査）。

透析導入の原因となった疾患（原疾患）を、糖尿病性腎症、腎硬化症、慢性糸球体腎炎、その他の４つに分けて検討した結果も同様で、原疾患によらず、透析導入患者では肥満者の割合が増加し、低体重の割合が低下している経年変化が認められた。

②腎生検割合

2023 年の透析導入患者のうち，「生検等により確認された原疾患」は 2,014 人（男性 1,319 人，女性 695 人）と，腎生検割合はわずか男性 5%，女性 6%であった。この割合は 2006 年から不変であったが，原疾患に検討すると、慢性糸球体腎炎の透析導入患者では，男女とも 2006 年の 8%から 2023 年の 16%へと増加傾向を認めた（下図）。

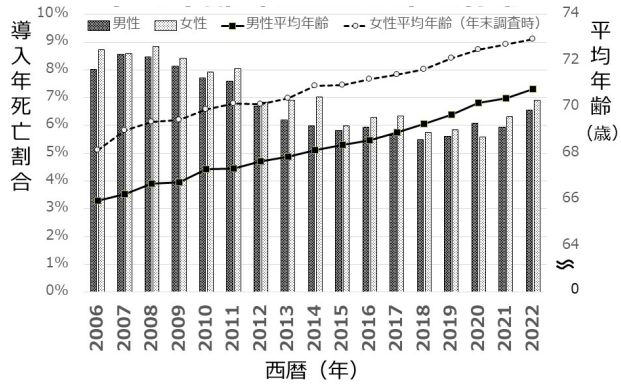


一方、原疾患が糖尿病性腎症や腎硬化症では、腎生検割合は 2006 年から 2023 年まで男女とも不変であった。

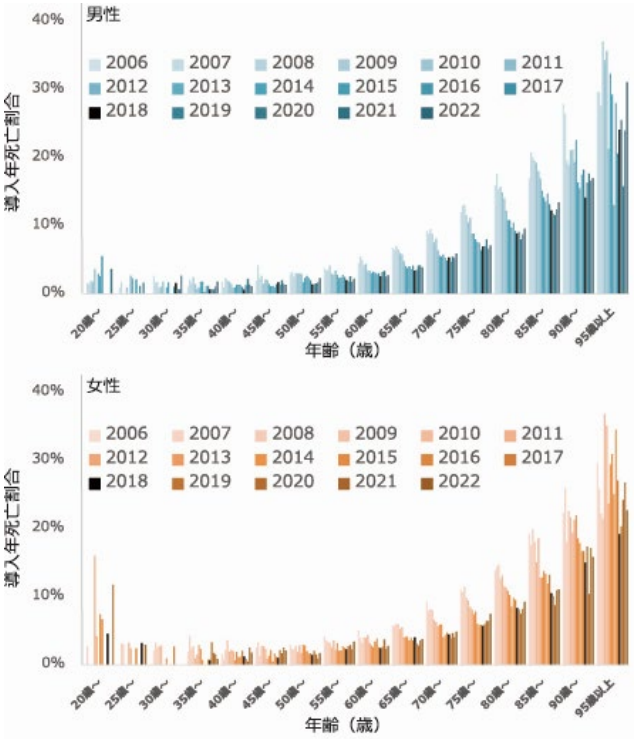
③導入年死亡

2023 年の透析導入患者のうち，導入された年に死亡した患者数は 2,467 人（男性 1,734 人，女性 733 人）と，導入年死亡割合は男女とも 7%であった。透析導入日により観察期間がさまざまではあるが，透析導入患者 100 人のうち 7 人は透析導入された年に死亡している計算になる。

この導入年死亡割合は，2007 年には 9%であったが，2018 年には男性 5%，女性 6% まで低下し，その後，緩やかに上昇し，現在は男女とも 7%であった（下図）。



2022 年末調査までのデータで年齢階級別に検討すると，導入年死亡割合は男女とも加齢に伴い高くなり（下図），最も導入年死亡割合が高い 95 歳以上では，男性は 31%，女性は 23%であった（2022 年末データ）。



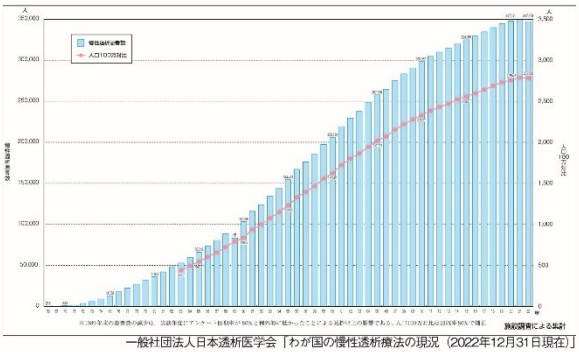
経年変化をみると，男女とも 2006 年頃に比べて幅広い年齢層で改善していた。

D. 考察

１）透析患者総数・新規導入患者数の推移

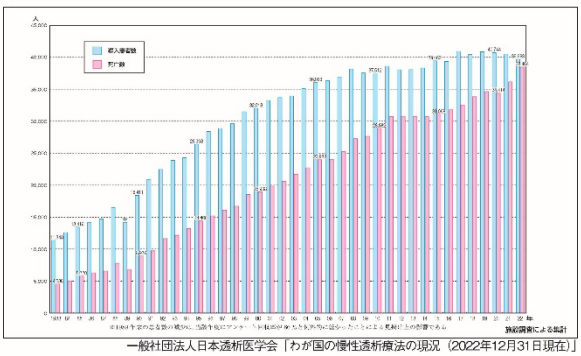
①2023 年末までの調査結果より

日本透析医学会統計調査委員会の公開データより、維持透析患者数は 2020 年より 35 万人弱の横ばい状態となっている。



一般社団法人日本透析医学会「わが国の慢性透析療法の現況（2022年12月31日現在）」

また新規透析導入患者数も 2019 年をピークに漸減傾向となっている。

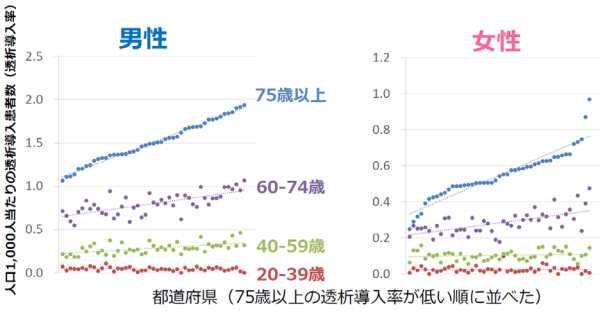


一般社団法人日本透析医学会「わが国の慢性透析療法の現況（2022年12月31日現在）」

これらの調査結果は腎疾患対策検討会報告書の全体目標に沿った転帰となっており、この結果は CKD 重症化予防に加え、新型コロナウイルスパンデミック、保存的腎臓療法を選択する患者数や腎移植件数の増加の複合的な要因が想定される。その内、CKD 重症化予防に関しては、本研究班の取り組みを含むオールジャパンの CKD 対策による CKD 進展抑制の成果と考えられる。

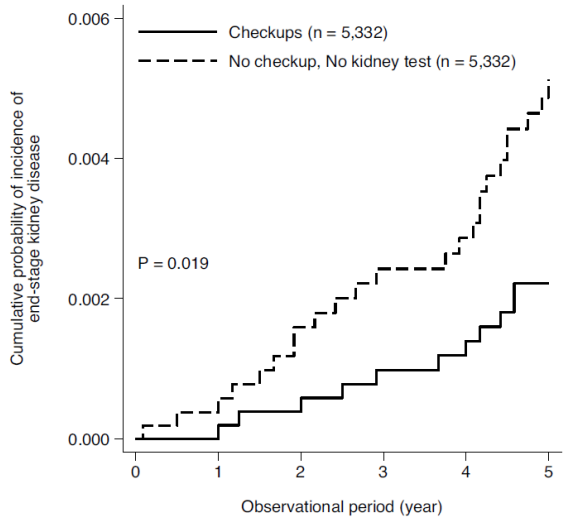
②都道府県別透析導入率に影響する要因

年齢階級別にみると、75 歳以上の透析導入率は都道府県により男性は約 2 倍、女性は約 4 倍の差を認め、透析導入率が高い都道府県ではその前の年齢階級の透析導入率も高い傾向がみられた。



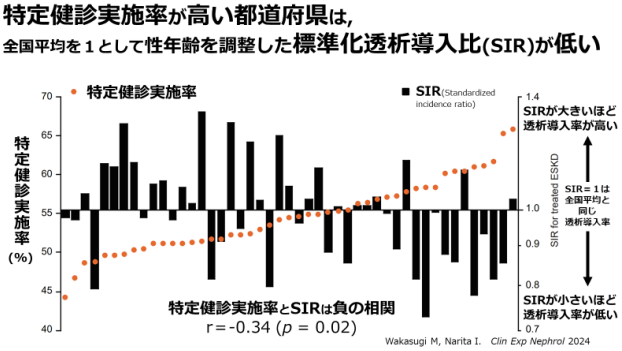
男性を例に示すと、75 歳以上の都道府県別・男性透析導入率は、60－74 歳の都道府県別・男性透析導入率と正の相関を示し（R^2＝0.52）、60－74 歳の都道府県別・男性透析導入率は、40－59 歳の都道府県別・男性透析導入率と正の相関を示していた（R^2＝0.54）。なお、40－59 歳の都道府県別・男性透析導入率と 20－39 歳では相関を認めなかった（R^2＝0.007）。女性でも同様の関係性が認められた。以上より、75 歳以上の透析導入率が高い都道府県は、その前の年代（40-74 歳）から透析導入率が高いことから、75 歳以上の透析導入率の都道府県差を小さくするためには、その前の年代（40-74 歳）からの介入が効果的と考えられた。

透析導入率の地域差を説明する因子として、大阪大学と大阪府寝屋川市との共同研究の成果として（下図）、男性において特定健診未受診者（破線）は受診者（実線）に比較して有意に透析導入率が高いことが示され、この関連性は女性では認められなかった。



(Yoshimura R, et al. Sci Rep 2021;11:20717)

そこで都道府県別透析導入率を、性年齢を調整し全国平均を 100%とした標準化透析導入比で示すと 73%から 134%と、都道府県により異なり特定健診の都道府県別実施率と負の相関を示していた（下図）。

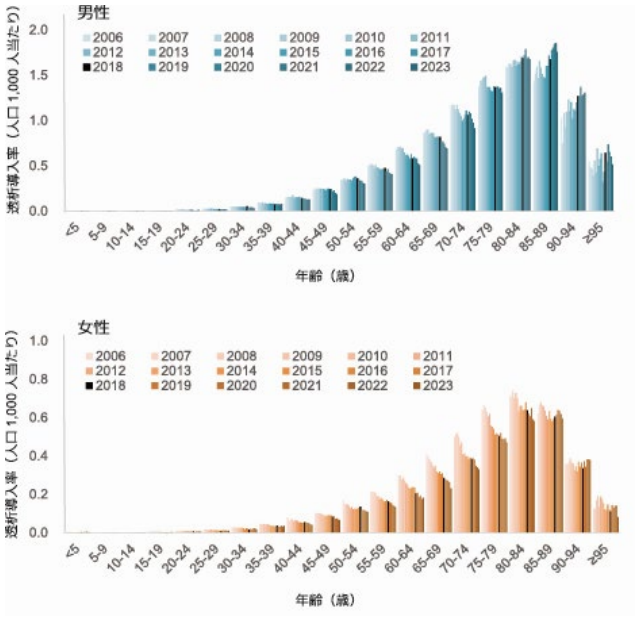


(Wakasugi M, et al. Clin Exp Nephrol 2024;28:201)（資料３）

特定健診受診者における都道府県別 CKD 有病率は 11%から 20%と、こちらも都道府県により異なり、特定健診実施率と負の相関を示していた。以上の結果より、特定健診実施率を高めることで 40-74 歳からの介入が増加し、CKD 有病率ならびに透析導入率を低下させる効果が示唆される。そこで今後も積極的な働きかけが重要と考えられる。

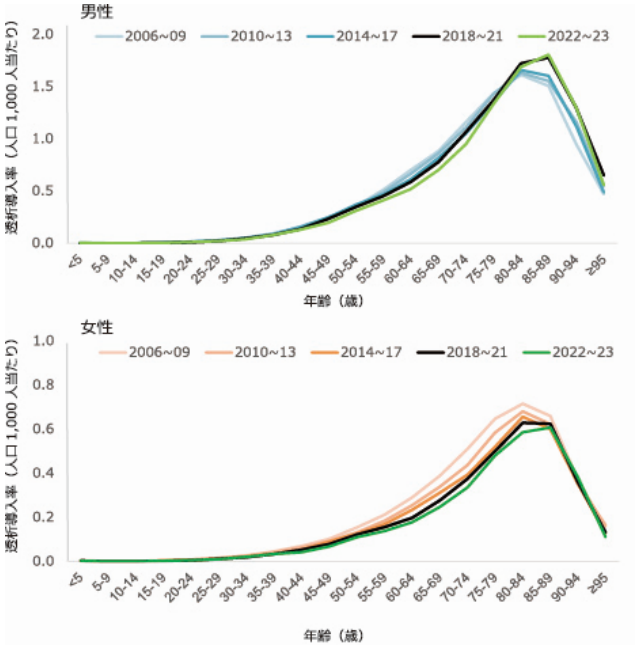
③ 透析導入率の年次推移

2023 年に報告した 2021 年までの透析導入率の経年変化に、2022 年と 2023 年のデータを加えた評価を行ったところ、男女とも性年齢階級別透析導入率はさらに低下傾向にあった（下図）。



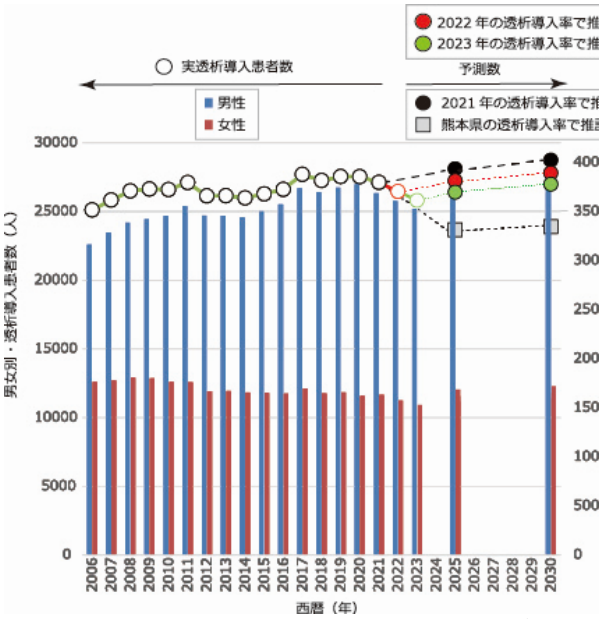
2023 年の検討（2006 年から 2021 年まで）では，黒で示した 2018 年（報告書発出年）以降，男女とも 80 歳未満では低下傾向，80 歳以上の男性で上昇傾向であったが，今回，2022～2023 年の透析導入率をグラフに加えると，80 歳以上の男性も低下傾向にあった。

経年変化を視覚的にわかりやすくするため，4 年毎にまとめたグラフ（下図）では，前回の検討と同様，年々，グラフが全体的に右（高齢）の方へシフトしており，透析導入を先送りできていることが示唆された。



2023 年の検討で、黒線で示した 2018～2021 年の 4 年間では 80 歳以上の男性で透析導入率が上昇していたが，直近の 2 年間（2022～2023 年）はその上昇が抑えられていた。仮に透析導入率が現状（2023 年）のままなら，将来推計人口

（令和 5 年推計）から計算された透析導入患者数は，2025 年 36,959 人，2030 年 37,763 人と推計され，現状（2023 年）のままなら目標の 3 万 5 千人以下は達成されないと考えられた（下図）。



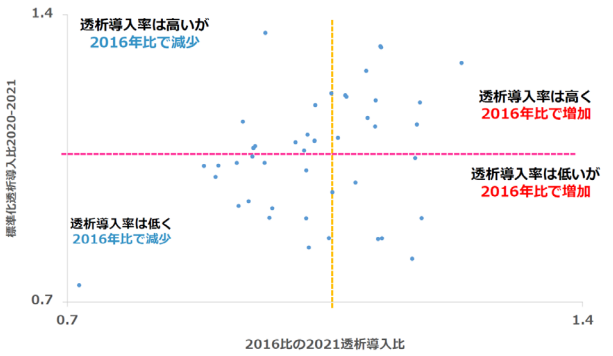
（日腎会誌 2024;66:333 より一部改変）（資料 4）

しかし，この人数は，2021 年の透析導入率を用いた 2023 年の検討（2025 年 39,319 人，2030 年 40,213 人）や，2022 年の透析導入率を用いた計算（2025 年 38,159 人，2030 年 38,945 人）よりも少なくなっていた。すなわち，年々，KPI 達成に近づいていると考えられた。

2）本研究班の達成度の今後の展望

本研究班の研究目的に関して、CKD の普及・啓発については啓発活動の結果、順調に普及が進んでいる。診療連携体制構築については都道府県で進捗に格差はあるものの、方向性は共有されており、今後は好事例の横展開を促進したい。診療水準の向上については客観的な指標による評価が不十分であるものの、標準治療の普及は進んでいると想定される。人材育成についても順調に腎臓病療養指導士数は増えており、保健師による CKD ケアへの参入も促進された。研究開発については十分な成果が示されたと判断する。よって研究班の計画した目的はほぼ到達したものと考える。

本研究班の成果から CKD 対策の注力ポイントとしては、特定健診の受診勧奨と病診連携体制構築・運用の横展開（かかりつけ医から腎臓専門医への紹介ステージの前倒しを含む）が重要と考えられる。その効率的な介入方法として、透析導入率が高くかつ 2016 年度比でも増加傾向である地域（下図の右上区分に位置する県）を優先的な対象地域としていく。



また研究開発の目標としては、増加する透析導入原疾患である腎硬化症の進行因子を J-CKD-DBEx を用いて明らかとし、治療・管理方法の開発の一助とする。腎硬化症の重症度評価や治療効果の見える化には eGFR スロープが必須であり、並行して日常診療への eGFR スロープの導入を推進していく。

E. 結論

本研究班の活動は腎疾患対策検討会報告書が掲げた全体目標の達成のために有効に機能し、日本の新規透析導入患者数の減少に貢献した。2028 年の達成に向けて、より効率的な取り組みの継続が望まれる。

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G. 知的財産権の出願・登録状況
（予定を含む。）

1. 特許取得
なし
2. 実用新案登録
なし
3.その他
なし

別添４

研究成果の刊行に関する一覧表

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PLOS ONE

RESEARCH ARTICLE

Development of a prognostic risk score to predict early mortality in incident elderly Japanese hemodialysis patients

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Abstract

Background

Information of short-term prognosis after hemodialysis (HD) introduction is important for elderly patients with chronic kidney disease (CKD) and their families choosing a modality of renal replacement therapy. Therefore, we developed a risk score to predict early mortality in incident elderly Japanese hemodialysis patients.

Materials and methods

We analyzed data of incident elderly HD patients from a nationwide cohort study of the Japanese Society for Dialysis Therapy Renal Data Registry (JRDR) to develop a prognostic risk score. Candidate risk factors for early death within 1 year was evaluated using multivariate logistic regression analysis. The risk score was developed by summing up points derived from parameter estimate values of independent risk factors. The association between risk score and early death was tested using Cox proportional hazards models. This risk score was validated twice by using an internal validation cohort derived from the JRDR and an external validation cohort collected for this study.

Results

Using the development cohort (n = 2,000), nine risk factors were retained in the risk score: older age (>85), yes = 2, no = 0; sex, male = 2, female = 0; lower body mass index (<20), yes = 2, no = 0; cancer, yes = 1, no = 0; dementia, yes = 3, no = 0; lower creatinine (<6.5

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mg/dL), yes = 1, no = 0; lower albumin (<3.0 g/dL), yes = 3, no = 0; normal or high calcium (≥8.5 mg/dL), yes = 1, no = 0; and higher C reactive protein (>2.0 mg/dL), yes = 2, no = 0. In the internal and external validation cohorts (n = 739, 140, respectively), the medium- and high-risk groups (total score, 6 to 10 and 11 or more, respectively) showed significantly higher risk of early death than the low-risk group (total score, 0 to 5) (p<0.001).

Conclusion

We developed a prognostic risk score predicting early death within 1 year in incident elderly Japanese HD patients, which may help detect elderly patients with a high-risk of early death after HD introduction.

Introduction

Hemodialysis (HD) is an essential life-saving treatment for patients with end-stage kidney disease (ESKD); however, its usefulness is not being fully utilized in an increasing number of elderly patients with systemic complications such as ischemic heart disease, cognitive impairment, and frailty, who often experience rapid decline in activity of daily living (ADL) and deterioration in quality of life (QOL) after HD introduction [1,2]. Patients and their families sometimes regret the decision to introduce HD or wish to discontinue it. Although the long-term prognosis of maintenance HD patients in Japan is among the best in the world, the short-term prognosis in the first 4 months after introduction of HD is comparable to that in other countries [3]. Especially for patients aged 80 years or older, the mortality rate in the first 12 months after introduction reaches 30%, and about half of these patients die within 3 months after introduction [4]. When choosing a modality in renal replacement therapy (RRT), it is desirable that patients, their families, and medical professionals, including physicians, meet for shared decision-making (SDM), where all treatment options of RRT, including forgoing dialysis and conservative kidney management (CKM), are presented and the outcome of each option should be concretely explained [5,6]. For elderly patients and their families, information about short-term rather than long-term prognosis is more informative when choosing between maintenance dialysis and CKM. In foreign countries where CKM has been presented at SDM sessions for a longer time than in Japan, many prognostic models predict life expectancy in elderly patients with CKD who opt for HD [7–22]. Unfortunately, there have been very few reports regarding that for CKM [23].

In this study, we attempted to identify risk factors associated with early mortality within 1 year of HD introduction in elderly patients with CKD aged 75 years or older, and to develop a prognostic equation for life expectancy using the results of a nationwide cohort study of incident HD patients in Japan in 2006 and 2007.

Materials and methods

Development and internal validation cohort

Japanese Society of Dialysis Therapy (JSDT) has been conducting annual surveys of >99% of all HD facilities in Japan: JSDT Renal Data Registry (JRDR). In 2006 and 2007, JRDR collected incident HD patient data just prior to the time of HD introduction, and stored follow-up data on post-introduction survival for all the patients. Therefore, we used JRDR data from 2006

and 2007 to create a prognostic risk score to predict early mortality in incident elderly HD patients.

We obtained the anonymous data from JRDR in October, 2019. All 2,739 patients who initiated incident HD in 2006 and 2007 were enrolled using the following exclusion criteria (Fig 1): age <75 years, withdrawal from HD because of kidney transplantation and transition to peritoneal dialysis (PD), and missing values such as laboratory data. The included patients were randomly classified into two groups to obtain datasets of the development cohort (2,000) and internal validation cohort (739).

External validation cohort

Between March 2020 and March 2021, the incident elderly HD patients aged 75 or older (n = 140) were enrolled in a prospective, external validation cohort at six university hospitals scattered geographically in Japan (Saitama Medical University, Niigata University, Toho University, Osaka University, Kawasaki Medical School, Kurume University), and followed-up until March 2022.

Patient data

The datasets of the development and internal validation cohorts and the external cohort contained the following variables: sex; age; body mass index (BMI); comorbidities of cardiovascular disease (CVD) consisting of congestive heart failure and coronary arterial disease, any cancer and dementia determined by the attending physician to have any cognitive impairment; diabetic kidney disease (DKD) as a primary kidney disease; serum albumin, urea nitrogen (UN), creatinine (Cr), inorganic phosphorus (Pi), calcium (Ca), and C reactive protein (CRP) levels; hemoglobin (Hb) level; and presence or absence of arterio-venous fistula (AVF).

For the convenience of clinical practical use, all continuous variables were converted to binary categorical variables for prognostic risk score construction; age (super-elderly, defined as $\geq$ 85 years (yes = 1, no = 0)), BMI (underweight, defined as $<$ 20 (yes = 1, no = 0)), UN (low, defined as $<$ 65 mg/dL (yes = 1, no = 0)), Cr (low, defined as $<$ 6.5 mg/dL (yes = 1, no = 0)), Albumin (low, defined as $<$ 3.0 g/dL (yes = 1, no = 0)), Ca (normal or high, defined as $\geq$ 8.5 mg/dL (yes = 1, no = 0)), Pi (high, defined as $\geq$ 3.5 mg/dL (yes = 1, no = 0)), CRP (high, defined as $\geq$ 2.0 mg/dL (yes = 1, no = 0)) and Hb (low, defined as $<$ 10 g/dL (yes = 1, no = 0)). The cutoff values used to convert UN and Cr to binary categories were based on the average estimated glomerular filtration rate (eGFR) (5 mL/min/1.73m^2) at the time of incident HD in Japan [24]. Others were determined with reference to the common/target values for patients undergoing maintenance HD [25,26].

The primary outcome was early death, defined as all-cause death with 1 year of HD introduction. The JRDR data contained dates of death for all patients who died. For the external validation cohort, the dates of death were recorded. If no outcomes were observed within the follow-up period, the observation data were treated as censored data.

Statistical analysis

Normally distributed, continuous variables are presented as mean ± standard deviation (SD); otherwise, the median and interquartile range are presented. Intergroup comparisons of variables were performed using Chi-squared test, t-test, and Mann-Whitney U test, as appropriate.

The analyses were conducted using EZR version 1.63 (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria, version 2.13.0) [27]. Statistical significance was defined as $p<0.05$.

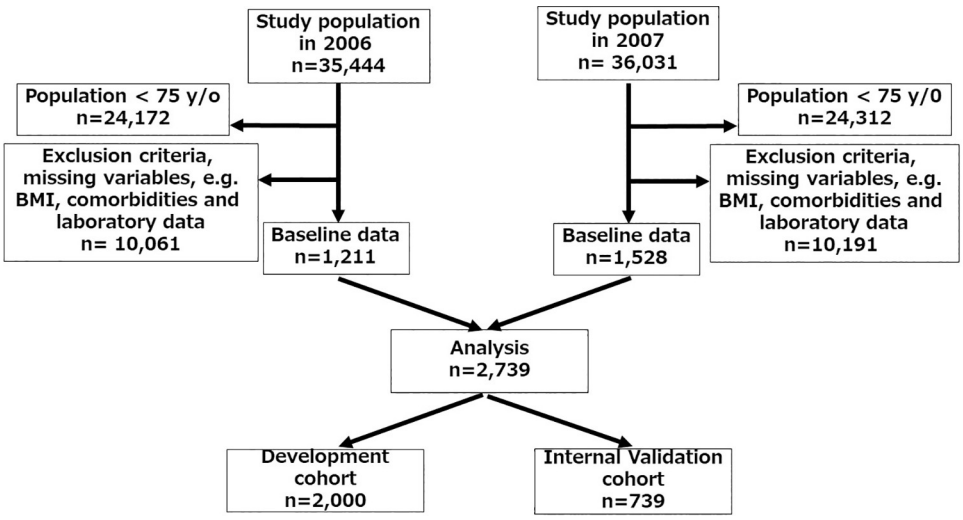

Fig 1. Flow diagram of the study population.

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Development of risk score

Using the development cohort dataset, univariate and multivariate logistic regression analyses were performed to identify risk factors significantly and independently associated with early death within 1 year in incident HD patients. Collinearity was tested using variance inflation factor (VIF), and variables with VIF≥2 were omitted because of collinearity.

A weighted score proportional to the smallest parameter estimate of the independent risk factors was assigned to each categorical index, which was rounded to the nearest integer. For each patient, the risk score was calculated as the sum of the points.

Based on categorical criteria for the risk score, the patients were divided into three risk groups using Kaplan-Meier survival curves: low-, medium-, and high-risk. Then, the survival probabilities of the groups were compared using log-rank test. Moreover, the risk of the outcome was compared between risk groups by Cox proportional hazards models adjusted for baseline characteristics not included in the risk score. The proportional hazards assumption was graphically verified using log-log plots. Results of statistical analyses are presented as hazard ratios (HRs) with 95% confidence of intervals (CI), as appropriate.

Validation of risk score

The accuracy of the prediction of the outcome of the risk score was evaluated on the basis of area under the receiver operating characteristic (ROC) curve (AUC) and c-statistics using datasets from the internal validation as well as the external validation cohort. Additionally, the risk score was validated using Kaplan-Meier survival curves and Cox proportional hazard models as described above.

Ethics

The development and internal validation cohort study was approved by the ethics committee of JSDT (JSDT No.2) and was exempt from the need to obtain informed consent from participants. The external validation cohort study was approved by the Institutional Review Board of Saitama Medical University (19091.01) as a base facility for this multi-center collaborative research, and we obtained informed consent from all the participants.

All data were analyzed anonymously. The study was performed in accordance with the Declaration of Helsinki (revised 2013) and the ethical guidelines for medical and health research involving human subjects by the Japanese Ministry of Health, Labour and Welfare (revised 2023).

Results

Baseline characteristics

The final study population consisted of 2,739 patients (Fig 1), and 424 deaths occurred within 1 year of the follow-up period. Causes of death included infection in 102 patients, congestive heart failure in 80, malignancy in 35, stroke in 30, cardiovascular disease in 14, and unknown in 163. Baseline demographic and clinical characteristics of the study population by primary endpoint are shown in Table 1.

The study population was randomly assigned into two cohort groups: one group for the development cohort and the other for the internal validation cohort (Fig 1). No significant differences in baseline patient characteristics between the datasets of the development and internal validation cohorts were observed (Table 2). The baseline patient characteristics of the external validation cohort are shown in Table 3.

Independent risk factors for early death within 1 year

Using the dataset of the development cohort, univariate logistic regression analyses were performed, and some of variables were significantly associated with early death within 1 year in

Table 1. Comparison of patient characteristics and laboratory data of the study population at incident hemodialysis by primary endpoint.

Basic characteristics	All	Survive ≥ 1 year	Death <1 year	p-value
N	2,739	2,315	424	
Sex (Male) (%)	1,570 (57.3)	1.317 (56.8)	253 (59.7)	0.31
Age (years)	80 (77, 83)	80 (77, 83)	81 (78, 85)	<0.001
BMI (kg/m2)	21.8±3.9	22.0±3.9	20.9±3.8	<0.001
Primary kidney disease				
DKD (%)	1,092 (39.9)	936 (40.4)	156 (36.8)	0.16
CGN (%)	633 (23.1)	531 (22.9)	102 (24.1)	0.62
PKD (%)	43 (1.6)	12 (0.5)	6 (1.4)	1.00
Nephrotic (%)	8 (0.3)	8 (0.3)	0	0.62
Others (%)	963 (35.1)	836 (35.9)	160 (37.7)	0.25
Laboratory data				
UN (mg/dl)	86.4±30.4	86.4±30.0	86.9±32.4	0.77
Cr (mg/dl)	7.3±2.9	7.4±2.8	6.8±3.2	<0.001
Albumin (g/dL)	3.2±0.6	3.3±0.6	3.0±0.6	<0.001
Ca (mg/dl)	7.9±1.0	8.0±1.0	8.0±1.2	0.22
Pi (mg/dl)	5.3±1.6	5.4±1.6	4.9±2.0	0.06
CRP (mg/dl)	0.46 (0.1, 2.1)	0.34 (0.1, 1.6)	1.72 (0.4, 4.8))	<0.001
Hb (g/dl)	8.4±1.5	8.4±1.5	8.4±1.6	0.99
AVF (%)	1,465 (53.5)	1,332 (57.5)	133 (31.3)	<0.001
Comorbidities				
CVD (%)	255 (9.3)	206 (8.9)	49 (11.6)	0.08
Cancer (%)	196 (7.2)	149 (6.4)	47 (11.1)	0.001
Dementia (%)	453 (16.5)	323 (14.0)	130 (30.7)	<0.001
HD Duration (month)			6.1±3.7	

https://doi.org/10.1371/journal.pone.0302101.t001

Table 2. Comparison of patient characteristics and laboratory data of the study population randomly divided to the development and internal validation cohorts.

Baseline characteristics	All	Development	Internal Validation	p-value
N	2,739	2000	739	
Sex (Male) (%)	1,570 (57.3)	1153 (57.7)	417(56.4)	0.57
Age (years)	80 (77, 83)	80 (77, 83)	80 (77, 83)	0.32
BMI (kg/m2)	21.8±3.9	21.9±4.0	21.8±3.6	0.90
Primary kidney disease				
DKD (%)	1,092(39.9)	811(40.6)	281(38.9)	0.24
Laboratory data				
UN (mg/dl)	86.4±30.4	86.8±30.2	85.6±31.0	0.37
Cr (mg/dl)	7.3±2.9	7.3±2.9	7.3±2.8	0.49
Albumin (g/dL)	3.2±0.6	3.2±0.6	3.2±0.6	0.76
Ca (mg/dl)	7.9±1.0	8.0±1.1	8.0±1.1	0.18
Pi (mg/dl)	5.3±1.6	5.3±1.6	5.3±1.6	0.55
CRP (mg/dl)	0.46 (0.1, 2.1)	0.46 (0.1, 2.08)	0.46 (0.1, 2.38)	0.36
Hb (g/dl)	8.4±1.5	8.3±1.5	8.4±1.4	0.18
Absence of AVF(%)	1,274(46.5)	928(46.4)	346(46.8)	0.86
Comorbidities				
CVD (%)	255 (9.3)	192 (9.6)	63 (8.5)	0.42
Cancer (%)	196 (7.2)	146 (7.3)	50 (6.8)	0.68
Dementia (%)	453 (16.5)	342 (17.1)	111 (15.0)	0.20
Death<1 year(%)	424 (15.5)	313(15.7)	111(15.0)	0.72

https://doi.org/10.1371/journal.pone.0302101.t002

Table 3. Patient characteristics and laboratory data of the external validation cohort.

Baseline characteristics.	
N	140
Gender (Male) (%)	87 (62.1)
Age (years)	81 (78, 84)
BMI (kg/m2)	22.4±3.9
Primary kidney disease	
DKD (%)	55 (39.3)
Laboratory data	
UN (mg/dl)	86.1±27.1
Cr (mg/dl)	7.3±2.2
Albumin (g/dL)	3.2±0.6
Ca (mg/dl)	8.5±0.8
Pi (mg/dl)	5.4±1.4
CRP (mg/dl)	0.32 (0.1, 1.09)
Hb (g/dl)	10.1±6.9
Absence of AVF (%)	47 (33.6)
Comorbidities	
CVD (%)	34 (24.3)
Cancer (%)	15 (10.7)
Dementia (%)	55 (39.3)
Death<1 year (%)	18 (12.9)

https://doi.org/10.1371/journal.pone.0302101.t003

Table 4. Results of univariate logistic regression analysis of the development cohort.

Baseline characteristics	OR	95%CI	p-value
Age (years) ≧85	2.25	1.72, 2.95	<0.001
Sex (Male)	1.36	1.06, 1.75	0.015
BMI (kg/m2) <20	1.96	1.53, 2.51	<0.001
DKD: Yes	0.94	0.73, 1.20	0.623
Laboratory variables			
UN (mg/dl) <65	1.13	0.85, 1.49	0.406
Cr (mg/dl) <6.5	1.57	1.23, 2.00	<0.001
Albumin (g/dL) <3.0	2.67	2.09, 3.42	<0.001
Ca (mg/dl) ≥ 8.5	1.08	0.83, 1.42	0.563
Pi (mg/dl) ≥ 3.5	0.55	0.39, 0.80	0.001
CRP (mg/dl) ≧2.0	2.96	2.30, 3.80	<0.001
Hb (g/dl) <10	0.92	0.65, 1.29	0.617
Absence of AVF no	3.39	2.61, 4.41	<0.001
Comorbidities			
CVD yes	1.28	0.87, 1.87	0.215
Cancer yes	1.79	1.20, 2.67	0.005
Dementia yes	2.80	2.13, 3.69	<0.001

https://doi.org/10.1371/journal.pone.0302101.t004

incident elderly HD patients (Table 4). To create the risk score, subsequent multivariate logistic regression analyses were performed, and variables such as older age (>85), male sex, lower BMI (<20), cancer (Yes), dementia (Yes), lower Cr (<6.5), lower albumin (<3.0), normal or high Ca (≥8.5), and higher CRP (>2.0) were found to be significantly and independently associated with early death (Table 5). No collinearity was seen for all the variables being used.

Development of risk score

The score point was determined for each risk factor (Table 6).

The patients were categorized into three groups based on the risk score: low-risk, 0 to 5; medium-risk, 6 to 10; high-risk, 11 or higher. The Kaplan-Meier survival curve showed a significant difference between the groups (log-rank test, $p<0.001$) (Fig 2). The medium- and high-risk groups showed higher risks of early death within 1 year than the low-risk group (Table 7).

Validation of risk score

This prognostic risk score showed high accuracy for the prediction of the outcome in the internal validation cohort; c-statistics, 0.70 (95% CI, 0.64, 0.75), as well as in the external validation cohort; c-statistics, 0.87 (95% CI, 0.80, 0.94) (Figs 3A and 4A). Additionally, the Kaplan-Meier survival curves for early death within 1 year showed significant differences between the groups in the internal validation cohort (log-rank test, $p<0.001$) and in the external validation cohort (log-rank test, $p<0.001$) (Figs 3B and 4B). In the internal validation cohort, the risks of early death in the medium- and high-risk groups were significantly higher than those in the low-risk group according to Cox proportional hazards models (Table 8).

Since no events were observed in the low-risk group of the external validation cohort, the low- and the medium-risk groups were combined and used as the reference (Fig 4C and Table 9). The high-risk group showed approximately eight-times higher risk compared to the low-medium risk group.

Table 5. Results of multivariate logistic regression analysis of the development cohort.

Variables	Parameter estimates	aOR (95%CI)	p-value
Age (years) ≥ 85	0.733	2.08 (1.54, 2.81)	<0.001
Sex (Male)	0.520	1.68 (1.27, 2.22)	<0.001
BMI (kg/m2) < 20	0.632	1.88 (1.43, 2.47)	<0.001
Primary disease: DKD yes	-0.095	0.91 (0.69, 1.19)	0.489
Laboratory data			
UN (mg/dl) < 65	-0.036	0.97 (0.70, 1.34)	0.828
Cr (mg/dl) < 6.5	0.302	1.35 (1.02, 1.80)	0.037
Albumin (g/dL) < 3.0	0.771	2.16 (1.62, 2.85)	<0.001
Ca (mg/dl) ≥ 8.5	0.331	1.39 (1.02, 1.90)	0.035
Pi (mg/dl) ≥ 3.5	-0.11	0.90 (0.59, 1.36)	0.605
CRP (mg/dl) ≥ 2.0	0.743	2.10 (1.59, 2.78)	<0.001
Hb (g/dl) < 10	-0.060	0.94 (0.64, 1.38)	0.760
Absence of AVF no	0.963	2.62 (1.97, 3.48)	<0.001
Comorbidities			
CVD yes	0.107	1.11 (0.73, 1.69)	0.619
Cancer yes	0.451	1.57 (1.01, 2.44)	0.045
Dementia yes	0.798	2.22 (1.65, 3.00)	<0.001

Abbreviation: aOR, adjusted odds ratio.

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Discussion

In this study, we used data from cross-sectional and subsequent longitudinal surveys of incident HD patients in Japan in 2006 and 2007. We aimed to develop prognostic risk scores for predicting early mortality within 1 year after HD introduction in elderly patients with CKD aged 75 years or older. Robust results were observed in internal validation using an internal validation cohort and external validation using a prospective cohort of incident HD elderly patients from 2020 to 2021. These results suggest that this prognostic risk score can at present

Table 6. Parameter estimates of the independent risk factors and risk score points.

Variables	Parameter estimates	Ratio	Risk score point
Age (years) ≥ 85	0.733	2.42	2
Sex (Male)	0.520	1.72	2
BMI (kg/m2) < 20	0.632	2.10	2
Cr (mg/dl) < 6.5	0.302	1.0	1
Albumin (g/dL) < 3.0	0.771	2.55	3
Ca (mg/dl) ≥ 8.5	0.331	1.10	1
CRP (mg/dl) ≥ 2.0	0.743	2.46	2
Absence of AVF no	0.963	3.19	3
Cancer yes	0.451	1.49	1
Dementia yes	0.798	2.64	3

Risk score = older age + male sex + low BMI + low Cr + low albumin + normal or high Ca + high CRP + absence of AVF-no + cancer-yes + dementia-yes.

Older Age, yes = 2, no = 0; sex, male = 2, female = 0; low BMI, yes = 2, no = 0; low Cr, yes = 1, no = 0; low albumin, yes = 3, no = 0; normal or high Ca, yes = 1, no = 0; high CRP, yes = 2, no = 0; absence of AVF; no = 3, yes = 0; cancer, yes = 1, no = 0; dementia, yes = 3, no = 0.

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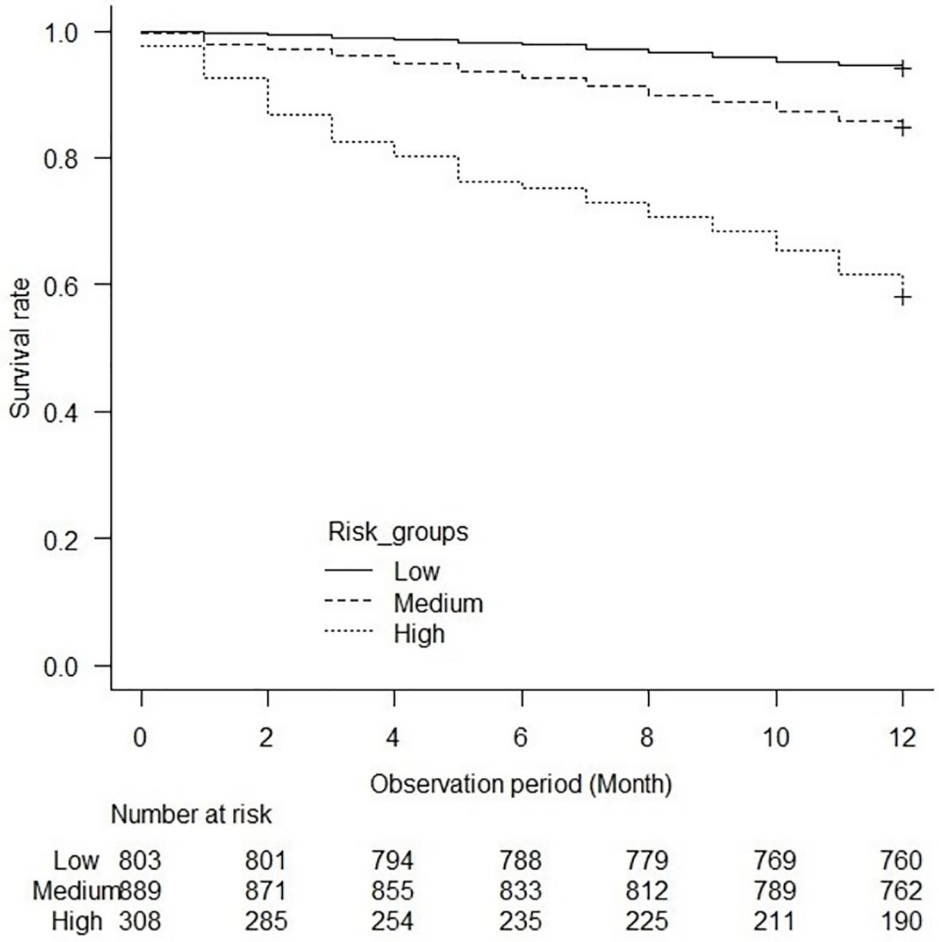

Fig 2. Association between the risk groups and mortality in the development cohort. The Kaplan-Meier survival curves show a significant difference in mortality between the risk groups (log-rank test, $p<0.001$).

https://doi.org/10.1371/journal.pone.0302101.g002

be used reliably to predict early mortality after HD introduction in elderly Japanese ESKD patients, when patients, their families, and health professionals are making SDM sessions for a choice of modality in RRT. However, as mentioned in the Introduction, there are very few scores to estimate the life expectancy of elderly ESKD patients who choose PD or CKM. Therefore, it is important to note that presenting only the life expectancy in case of HD without mentioning those in cases of PD and CKM may be a biased guidance.

Table 7. Risk groups and risk of early death within 1 year in the development cohort.

Risk groups	HR	aHR
Low-risk group	**Reference**	**Reference**
Medium-risk group	**2.69 (95CI, 1.94, 3.74; p<0.001)**	**2.67 (95%CI, 1.92, 3.71; p<0.001)**
High-risk group	**8.79 (95CI, 6.31, 12.24; p<0.001)**	**8.63 (95CI, 6.18, 12.07; p<0.001)**

Abbreviation: aHR, adjusted hazard ratio.

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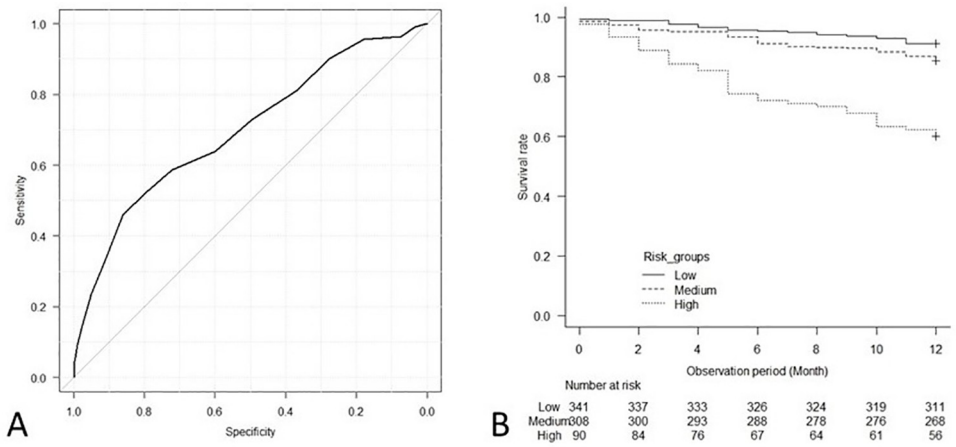

Fig 3. The ROC curve of the prognostic risk score for the prediction of early death within 1 year (A), and association between risk groups and mortality in the internal validation cohort (B). (A) The prognostic risk score showed high accuracy for the prediction of the outcome in the internal validation cohort; c-statistics, 0.70 (95% CI, 0.64, 0.75). (B) The Kaplan-Meier survival curves show a significant difference in mortality between the risk groups (log-rank test, $p<0.001$).

https://doi.org/10.1371/journal.pone.0302101.g003

In the 1990s, it became common for patients to be offered the option of not receiving dialysis or CKM during SDM sessions [5,6,28]. Since it is necessary to provide information on patient prognosis after the introduction of RRT [5,6], various attempts to predict prognosis have been reported. Even if we limit articles published since 2000 that deal with prognostic models that are still expected to be useful in terms of life expectancy, we found 21 articles that analyzed risk factors just prior to HD introduction as explanatory variables and early death within 1 year after HD introduction as an objective variable [4,7–22,29–32].

The groups of explanatory variables that were independently and significantly related to the early death were demographic data (age, sex, BMI), laboratory data (serum albumin, serum creatinine, eGFR, blood hemoglobin, CRP), therapeutic drugs, underlying diseases causing CKD, and comorbidities (CVD, malignancy, obstructive lung disease). Older age, male sex, high serum CRP levels, and comorbidity with cancer have been reported as risk factors for early death [4,8–22,29,31,32], and are consistent with the clinical experience, which seems satisfactory. Additionally, variables such as BMI and serum albumin, which are indicators of

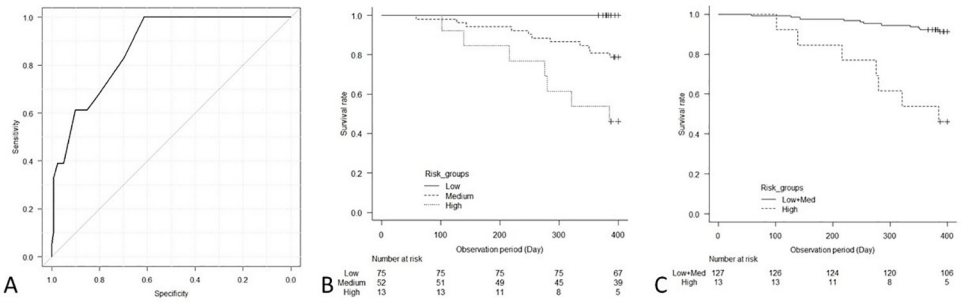

Fig 4. The ROC curve of the prognostic risk score for the prediction of early death within 1 year (A), and association between risk groups and mortality in the external validation cohort: Among three risk groups (B), among two risk groups (C). (A) The prognostic risk score showed high accuracy for the prediction of the outcome in the external validation cohort; c-statistics, 0.87 (95% CI, 0.80, 0.94). (B and C) In both analysis, Kaplan-Meier survival curves show significant differences in mortality between the risk groups (log-rank test, $p<0.001$).

https://doi.org/10.1371/journal.pone.0302101.g004

Table 8. Risk groups and risk of early death within 1 year in the internal validation cohort.

Risk groups	HR	aHR
Low-risk group	Reference	Reference
Medium-risk group	1.71 (95CI, 1.08, 2.71; p = 0.02)	1.63 (95%CI, 1.03, 2.60; p = 0.04)
High-risk group	5.53 (95CI, 3.41, 8.99; p<0.001)	5.21 (95CI, 3.18, 8.53; p<0.001)

https://doi.org/10.1371/journal.pone.0302101.t008

nutritional status, have been discussed in many reports [4,7,9–11,13,14,16,17,19,20,22,30–32]. HD introduction in the absence of AVF is also considered to lead to a significant risk of early death in many reports, and HD introduction in the absence of AVF may be used as an index that includes multiple risks of mortality [4,8–10,13,14,20,22,31]. All these are significant risk factors in our prognostic risk score. On the other hand, it is not clear why normal or high serum Ca levels remained a risk factor [32], and the possibility that they might be associated with undiagnosed malignancy cannot be ruled out. In addition, the reason why either DKD or CVD, which was often reported as a risk factor [5–18,20,22,29,32], was not one in this study may be that patients with DKD and/or CVD with poor general condition were not introduced to HD and not included in the study population.

In recent years, an increasing number of reports have demonstrated prognostic factors related to aging, such as physical impairment, cognitive impairment, poor nutrition, frailty, and fall episodes, as explanatory variables in predicting life expectancy of dialysis patients [33–35]. These risk factors are likely confounding because they are closely related to each other, and except for poor nutrition, they are rarely employed as independent explanatory variables in the same prognostic model. Serum creatinine as laboratory data is a significant explanatory variable in several prognostic models, but each report shows conflicting associations between residual renal function at dialysis introduction and early death within 1 year after introduction [4,8,14–17,20,29,30,32,36]. Among them, one report showed that when low serum creatinine, which indicates early introduction of dialysis, was a significant risk factor for death, such significance disappeared when adjusted for frailty, suggesting that frailty is strongly associated with death [36]. Frailty is strongly related to the prognosis of dialysis patients as a composite index including multiple risks of mortality [37], and it is desirable to develop improved frailty assessment criteria for patients with CKD [38]. Low serum creatinine is also a risk factor in our prognostic risk score and may be associated with sarcopenia, a precursor condition of frailty. Most of the prognostic models for aging-related factors have been reported from foreign countries, but there have been several reports from Japan on the degree of dependence on nursing care related to physical dysfunction [4,29,30,32]. Although cognitive impairment has not been addressed extensively [17], we employed dementia as a candidate risk factor to be significantly associated with early death in our prognostic risk score.

A systematic review on the prediction of short- to long-term life expectancy in incident HD patients was reported by Anderson et al. in 2019 [39]. Among their results, the ROC curves with the largest AUC as discriminative of life expectancy were the Ivory index and the Obi

Table 9. Risk groups and risk of early death within 1 year in the external validation cohort.

Risk groups	HR	aHR
Low and Medium-risk group	Reference	Reference
High-risk group	8.31 (95CI, 3.21, 21.52; p<0.001)	8.02 (95CI, 2.65, 24.28; p<0.001)

https://doi.org/10.1371/journal.pone.0302101.t009

index [16,17], both of which are useful with respect to predicting early death within 1 year. The latter in particular has shown robustness in external validation cohorts [17]. (http://www.dialysisscore.com/) The AUC of the ROC curve of our prognostic risk score were as discriminative as those of these indices.

The prognostic model of Inaguma et al. for Japanese patients is superior because of the size of the study population used to construct the prognostic model, the diversity of explanatory variables employed, and the high discriminative power for predicting early death within 1 year of HD introduction [32]. The difference between our risk score and theirs is that their model was based on the data collected from a limited region of Japan, while ours is based on national data. Additionally, the reliability of our prognostic risk score is further enhanced by the fact that a recent prospective cohort was constructed using data from all of Japan, and external validation was conducted using this cohort.

There are several limitations to this study. First, there may be selection bias due to the removal of a large number of patients with missing data from consideration. Second, the sample size became smaller because of the restriction of age and RRT modality. However, the number of HD patients who progressed to kidney transplant or PD was small and was removed from the study to make it easier to interpret the results. Third, although data were collected on important complications such as fluid overload, chronic pulmonary or liver disease, they could not be analyzed as candidate risk factors due to missing data or unknown responses. Fourth, although electrolytes other than Ca and Pi, medications, physical findings (e.g., blood pressure and physical function) and social settings are good candidate risk factors, those were not collected and thus not examined as risk factors. Therefore, this score could not be compared with existing models such as the Ivory index, Obi index and Inaguma et al. score [16,17,32]. The fifth is that this study did not examine ESKD patients who were not introduced to HD. Elderly ESKD patients who were introduced to HD are likely to be healthier than those not introduced. It is possible that DKD and CVD were not included as variables in the prognostic risk score because high-risk patients with DKD or CVD were not introduced to HD. Therefore, our prognostic risk score should be used with caution when generalizing to the entire population of elderly ESKD patients. Sixth, some information was lost because continuous variables were converted to binary categorical variables to create a clinically usable score. Seventh, there could be bias due to unintended confounding for an observational study. Eighth, because the observed endpoint was all-cause mortality, it was not possible to evaluate ADL prognosis and QOL, such as frail and bedridden patients.

In conclusion, we used nationwide cohort data to identify the major risk factors for early death within 1 year in incident elderly Japanese HD patients and developed a prognostic risk score in this study. The robustness of this prognostic risk score was confirmed by data from an internal validation cohort and a more recent prospective cohort, and future clinical applications are anticipated. In addition to the information provided by this prognostic risk score, we hope to provide information on the prognostic value of choosing PD or CKM, which will facilitate the decision making for elderly ESKD patients and their families regarding RRT modalities at SDM sessions.

Author Contributions

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Evaluating the associations between compliance with CKD guideline component metrics and renal outcomes

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Understanding the association between compliance to the Chronic Kidney Disease (CKD) guidelines in real-world clinical settings and renal outcomes remains a critical gap in knowledge. A comprehensive analysis was conducted using data from a national, multicenter CKD registry. This study included 4,455 patients with an estimated glomerular filtration rate (eGFR) measurement on the index date and eight additional metrics recorded within six months. These metrics comprised serum electrolyte levels, low-density lipoprotein cholesterol, hemoglobin, and the use of renin-angiotensin system inhibitors. The primary outcome was a composite of renal events, defined by a decline in eGFR to < 15 mL/min/1.73 m^2 or a reduction of ≥ 30% in eGFR, confirmed by follow-up tests. Over a median follow-up of 513 days, 838 renal events were observed. High serum potassium levels (> 5.4 mmol/L) were associated with increased event rates compared to lower levels. Similarly, low serum sodium-chloride levels (< 33) correlated with higher event rates. Usage of renin-angiotensin system inhibitors, low serum calcium (< 8.4 mg/dL), and high uric acid levels (> 7.0 mg/dL) were also linked to increased events. Conversely, higher hemoglobin levels (≥ 13 g/dL) were associated with lower event rates. Compliance to guidelines, categorized into quartiles based on the number of met metrics, revealed a significantly reduced risk of events in the highest compliance group (meeting 8 metrics) compared

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to the lowest (0–5 metrics). Compliance to CKD guidelines in clinical practice is significantly associated with improved renal outcomes, emphasizing the need for guideline-concordant care in the management of CKD.

Keywords CKD, Real-world clinical scenarios, Compliance to guidelines, Clinical questions, End-stage kidney disease

Abbreviations

CKD	Chronic kidney disease
CKD-EPI	Chronic kidney disease epidemiology collaboration
CIs	Confidence intervals
CQ	Clinical questions
eGFR	Estimated glomerular filtration rate
ESKD	End-stage kidney disease
HRs	Hazar ratios
ICD-10	International Classification of Diseases, Tenth Revision
J-CKD-DB	Japan Chronic Kidney Disease Database
LDL cholesterol	Low-density lipoprotein cholesterol
RAS inhibitor	Renin-angiotensin system inhibitor
SS-MIX2	Standardized Structured Medical Information Exchange 2

An emerging problem in both clinical and ambulatory medicine is chronic kidney disease (CKD)[1]. Approximately 13% of the Japanese adult population is estimated to have CKD[2]. CKD is known as not only a worldwide public health problem, but also a global socioeconomic concern. CKD encompasses many adverse outcomes including kidney failure, cardiovascular disease, and premature death[3]. Aging and lifestyle habits have an impact on kidney function. Japan is experiencing an increase in its elderly demographic, and it is projected that the incidence of CKD will rise correspondingly within this aging populace in the imminent future[4,5]. The number of end-stage kidney disease (ESKD) patients has also continued to increase in Japan[6,7].

Clinical practice guidelines aid many purposes. Guidelines help clinicians and other caregivers deal with the exponential growth in medical literature, help to expose gaps in knowledge, and suggest areas where additional research is needed[8]. Professional societies throughout the world decided that there is a need for developing clinical practice guidelines for patients with CKD because there are variations in the treatment approaches across different regions, leading to inconsistent patient outcomes. The Evidence-based Clinical Practice Guidelines for CKD 2018 and its associated guidelines[9–11] provides evidence-driven recommendations addressing clinical questions (CQ) related to CKD treatment in Japan. Yet, the actual compliance to that guideline in clinical settings within Japan remains unevaluated. Moreover, the association between this compliance rate and renal outcomes in CKD patients is undetermined. Identifying the association between compliance rates and renal outcomes in CKD patients is essential for advancing medical knowledge, improving patient care, informing healthcare policies, and ultimately enhancing the quality of life for individuals with CKD.

To bridge this research gap, our objective is to assess the degree of implementation of the guideline recommendations in real-world clinical scenarios and their subsequent associations with renal outcomes.

Results

A cohort of 11,333 individuals was identified as potential study participants. These individuals had undergone measurements for eight distinct component metrics pertaining to clinical questions, in addition to estimated glomerular filtration rate (eGFR) assessments. Of the 11,333 individuals, 146 individuals with a baseline eGFR below 15 mL/min/1.73m^2 were excluded. An additional 6,732 were removed due to lacking eGFR measurements after the index date, resulting in a final sample size of 4,455 individuals for the analysis. Participants included in this study were younger, had lower eGFR, were receiving renin-angiotensin system (RAS) inhibitors, and demonstrated reduced levels of calcium, phosphorus, and low-density lipoprotein (LDL) cholesterol at the index date e compared to those excluded from the analysis (Supplementary Table S1).

Table 1 details the baseline characteristics of the study participants: 53.5% were male, the average age was 67.2 years, and the mean eGFR was 54.6 mL/min/1.73 m^2. Patients underwent a median of 8 eGFR measurements, with the interquartile range spanning from 4 to 15. The median interval between these assessments was 60 days, with the interquartile range spanning from 38 to 92 days. Figure 1 illustrates the cumulative incidence of renal events across groups based on compliance to the 2018 CKD Clinical Practice Guidelines and its associated guidelines as follows[9–11]. In Fig. 1A, those with serum potassium > 5.4 mmol/L had higher event rates than those < 4.0 mmol/L and those between 4.0–5.4 mmol/L. In Fig. 1B, groups with serum sodium-chlorine < 33 had higher rates than those between 33–36 and > 36. In Fig. 1C, groups taking RAS inhibitors had higher rates than those not taking them. In Fig. 1D, groups with serum calcium < 8.4 mg/dL had higher rates than those ≥ 8.4 mg/dL. In Fig. 1F, groups with serum uric acid ≥ 7.0 mg/dL had higher rates than those < 7.0 mg/dL. Lastly, in Fig. 1H, groups with hemoglobin < 11 g/dL had the highest rates, followed by 11-13 g/dL and ≥ 13 g/dL. Analysis of renal event rates shows no significant difference in the cumulative incidence when comparing groups with serum phosphorus at or below 6.0 mg/dL and those below 6 (Fig. 1E), and between the groups with LDL cholesterol levels below and at or above 120 mg/dL (Fig. 1G).

Participants were categorized based on their compliance to the guidelines for each metric, distinguishing between those who complied and those who did not (Supplementary Table S2). During the median follow-up

Variables	Overall, n = 4,455
Age, years	67.2 ± 14.0
Men, %	2384 (53.5)
eGFR, mL/min/1.73m^2	54.6 ± 20.5
Potassium, mmol/L	4.3 ± 0.5
Sodium – Chlorine, mmol/L	35.6 ± 2.4
Use of RAS inhibitors, yes	1881 (42.2)
Calcium, mg/dL	9.1 ± 0.5
Phosphorus, mg/dL	3.3 ± 0.6
Uric acid, mg/dL	5.9 ± 1.5
Low-density lipoprotein cholesterol, mg/dL	104.3 ± 30.3
Hemoglobin, g/dL	13.0 ± 1.8
Hypertension, n (%)	3022 (67.8)
Diabetes mellitus, n (%)	3603 (80.9)
Glomerulonephritis, n (%)	895 (20.1)
Nephrotic syndrome, n (%)	581 (13.0)

Table 1. Baseline clinical characteristics at the index date. Data are expressed as means (standard deviations) or percentages. *eGFR* estimated glomerular filtration rate, *RAS* renin-angiotensin system.

period of 513 days, with an interquartile range of 213 to 959 days, there were 838 composite renal events. In unadjusted models, participants who demonstrated compliance with the guidelines, specifically in managing serum potassium, sodium-chloride, calcium, urine acid, and hemoglobin levels experienced fewer composite kidney events compared to their non-compliant counterparts (Table 2). In adjusted analyses, which simultaneously accounted for all seven metrics, as well as age, sex, and eGFR at the index date, participants who demonstrated compliance with the guidelines, specifically in managing serum potassium, sodium-chloride, calcium, and hemoglobin levels experienced fewer composite kidney events compared to their non-compliant counterparts (Table 2). In the adjusted model, we assessed whether the association between compliance to CKD guidelines and composite renal events varies based on the participants' eGFR levels above versus below 45 mL/min/1.73 m^2 at the index date. We identified a significant interaction (P = 0.01) based on eGFR levels at the index date, categorized as ≥ 45 mL/min/1.73 m^2 versus < 45 mL/min/1.73 m^2, in examining how compliance to LDL cholesterol guidelines was associated with renal event outcomes. Consequently, we conducted stratified analyses according to these eGFR categories at the index date. A difference in renal outcomes was evident between individuals with LDL cholesterol levels below 120 mg/dL and those with levels at or above this threshold, but this discrepancy was only apparent in the subgroup with eGFR levels below 45 mL/min/1.73 m^2 at the index date (hazard ratios [HRs] 0.75, 95% confidence intervals [CIs] 0.60 to 0.94).

Participants were categorized into quartiles based on their compliance to each metric, as detailed in Fig. S2. The quartiles were defined by scores of 0–5 points with n = 533 participants, 6 points with n = 1,304 participants, 7 points with n = 1,844 participants, and 8 points with n = 784 participants. During the follow-up period, 143 composite events, which included a decline in eGFR by ≥ 30% and ESKD, were recorded in the 0–5 point group. In contrast, the 8 point group witnessed 143 events, as detailed in Table 3. The 0–5 point group exhibited the highest cumulative incidence of composite events when compared to other quartiles (Fig. 2). In terms of the rate of composite events per 1,000 person-years, the 0–5 point group had the highest at 192, followed by the 6-point group at 110, the 7-point group at 90, and the 8-point group at 95. In an unadjusted model, the group with 6 points (HRs 0.55, 95% CIs 0.45 to 0.68), the group with 7 points (HRs 0.45, 95% CIs 0.37 to 0.54), and the group with 8 points (HRs 0.47, 95% CIs 0.38 to 0.60) had a significantly lower risk of composite events compared with the group with 0–5 points (Table 3). After multivariable adjustment, the HRs (95% CIs) for composite events were HRs 0.67 (95% CIs 0.54 to 0.83) for the group with 6 points, HRs 0.55 (95% CIs 0.45 to 0.67) for the group with 7 points, and HRs 0.55 (95% CIs 0.44 to 0.70) for the group with 8 points. The groups with 6, 7, and 8 points each had a statistically significant lower risk of a ≥ 30% decline in eGFR or ESKD when compared to the group with 0–5 points (Table 3).

Discussions

Our study is the first to utilize real-world data in a large-scale analysis of outcomes, demonstrating that compliance to CKD guidelines positively influences renal health. This assessment supports the efficacy of multidisciplinary therapeutic strategies, reinforcing the critical role of guideline-aligned care in CKD management.

The findings from our study indicate associations between electrolyte imbalances and the rates of adverse renal events. Specifically, groups with serum potassium > 5.4 mmol/L had higher event rates than those < 4.0 mmol/L and those between 4.0–5.4 mmol/L. Groups with a combined serum sodium-chloride level of less than 33 had higher event rates compared to those with levels within the 33–36 range and above 36. Additionally, groups with serum calcium levels below 8.4 mg/dL experienced higher event rates than those with levels of 8.4 mg/dL or higher. Serum phosphorus levels were consistently below 6.0 mg/dL across the observed cases, as instances of serum phosphorus reaching 6 mg/dL or higher were not detected in this cohort. This absence suggests a

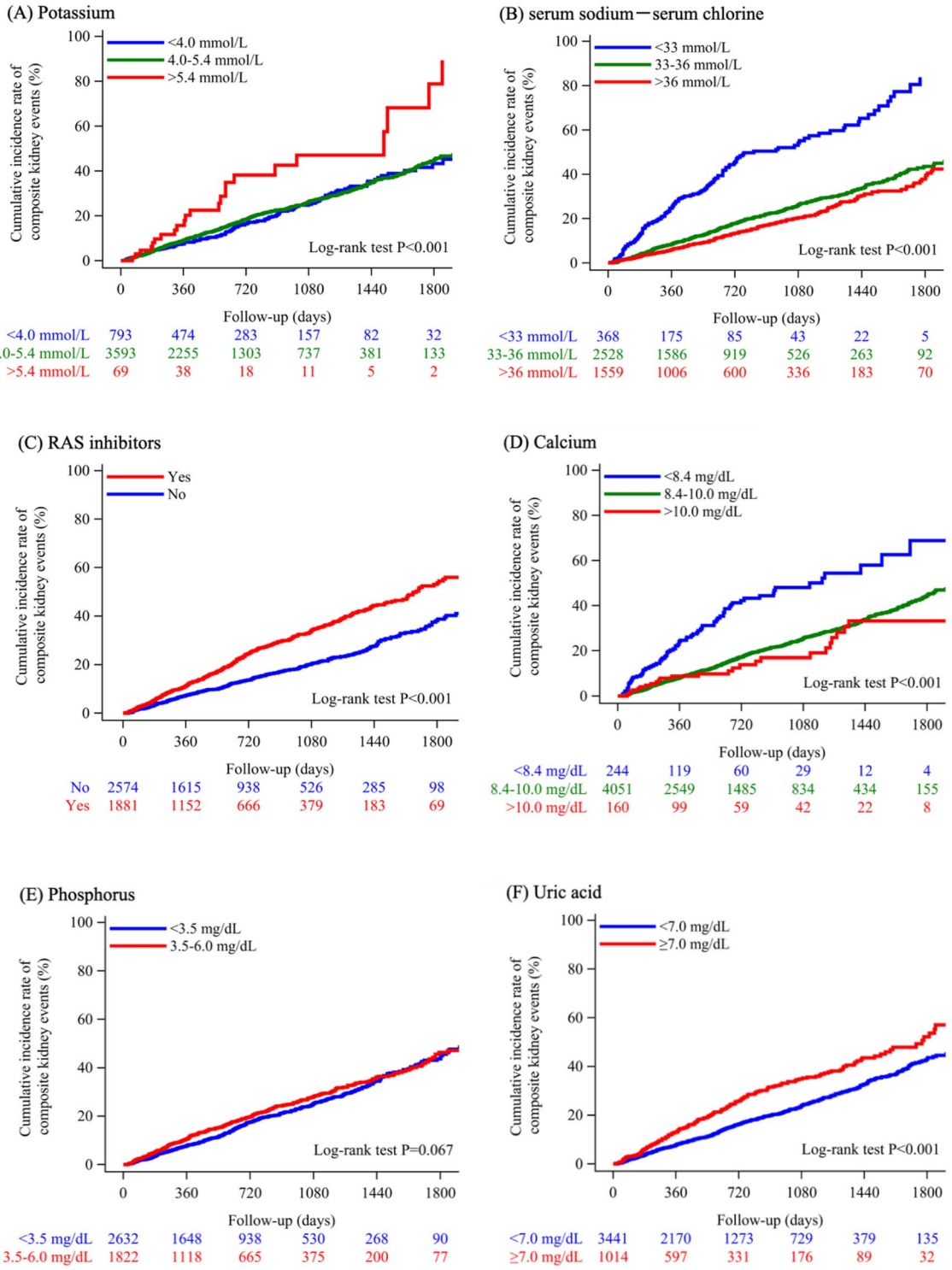

Figure 1. Cumulative incidence of composite renal events across groups of eight component metrics based on compliance to the 2018 CKD Clinical Practice Guidelines and its associated guidelines. We defined composite renal events as either the onset of ESKD, characterized by a decline in eGFR to less than 15 mL/min/1.73 m^2, or a reduction of 30% or more in eGFR from the index date, with both conditions requiring confirmation by follow-up tests. To evaluate the disparities in the cumulative incidence of the composite renal events among different groups that were categorized based on the compliance to the 2018 CKD Clinical Practice Guidelines and its associated guidelines, we applied the Kaplan–Meier method. Furthermore, we utilized the log-rank test to determine the statistical significance, as indicated by the P-value. CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; LDL cholesterol = low-density lipoprotein; RAS = renin-angiotensin system.

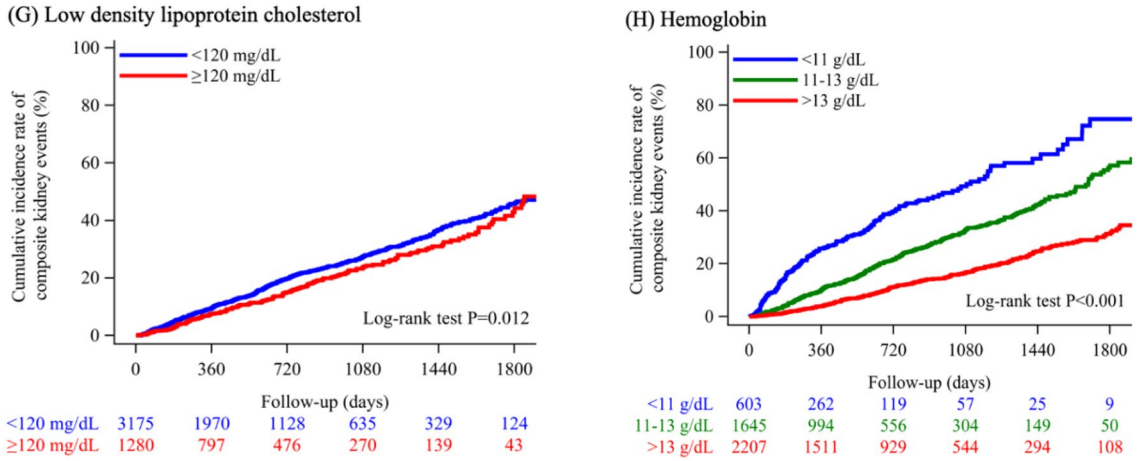

Figure 1. (continued)

Variables	Composite renal events	Unadjusted		Adjusted	
	Events/n	HRs (95% CIs)	*P* value	HRs (95% CIs)	*P* value
(A) Potassium					
> 5.4 mmol/L	23/69	1		1	
≤ 5.4 mmol/L	815/4386	0.46 (0.31, 0.70)	< 0.001	0.68 (0.44, 1.03)	0.067
(B) Sodium-Chlorine					
< 33 mmol/L	141/368	1		1	
≥ 33 mmol/L	697/4087	0.32 (0.27, 0.38)	< 0.001	0.57 (0.46, 0.69)	< 0.001
(C) Use of RAS inhibitors					
No	376/2574	1		1	
Yes	462/1881	1.73 (1.51, 1.98)	< 0.001	1.40 (1.21, 1.61)	< 0.001
(D) Calcium					
< 8.4 mg/dL	82/244	1		1	
≥ 8.4 mg/dL	756/4211	0.39 (0.31, 0.49)	< 0.001	0.56 (0.44, 0.71)	< 0.001
(E) Phosphorus					
> 6 mg/dL	0	-	-	-	-
≤ 6 mg/dL	838/4455				
(F) Uric acid					
≥ 7.0 mg/dL	244/1014	1		1	
< 7.0 mg/dL	594/3441	0.64 (0.56, 0.75)	< 0.001	0.85 (0.73, 1.00)	0.05
(G) Low-density lipoprotein cholesterol					
≥ 120 mg/dL	209/1280	1		1	
< 120 mg/dL	629/3175	1.22 (1.04, 1.43)	0.013	1.03 (0.88, 1.20)	0.748
(H) Hemoglobin					
< 11 g/dL	194/603	1		1	
≥ 11 g/dL	644/3852	0.32 (0.27, 0.38)	< 0.001	0.43 (0.36, 0.52)	< 0.001

Table 2. Associations between compliance to each of the eight specific metrics outlined in the 2018 Evidence-Based Clinical Practice Guidelines for CKD and its associated guidelines and composite renal events. Associations between adherence to each of the eight specific metrics outlined in the 2018 Evidence-Based Clinical Practice Guidelines for CKD and its associated guidelines and composite renal events in unadjusted and adjusted models. The median follow-up duration spanned 513 days and had an interquartile range from 213 to 959 days. Adjusted model included all eight metrics into the same model simultaneously, along with age, sex, and the estimated glomerular filtration rate at the index date. *CKD* chronic kidney diseases, *RAS* renin-angiotensin system, *HRs* Hazard ratios, *CIs* confidence intervals.

patient population with well-controlled phosphorus levels, potentially due to effective dietary management or treatment compliance. These results are suggestive within the context of previous studies[12–16], which have shown that electrolyte imbalances may have significant implications for renal outcomes. For instance, abnormal serum sodium and chloride levels are known to be associated with hypertension, cardiovascular events, and renal vasoconstriction[17], which could potentially lead to a decline in renal function over time. Furthermore,

Outcome	Point	n	Events	Unadjusted		Adjusted	
				HRs (95% CIs)	*P* value	HRs (95% CIs)	*P* value
Composite renal events	0–5	533	143	1.0	–	1.0	–
	6	1,304	243	0.55 (0.45–0.68)	< 0.001	0.67 (0.54–0.83)	< 0.001
	7	1,844	309	0.45 (0.37–0.54)	< 0.001	0.55 (0.45–0.67)	< 0.001
	8	784	143	0.47 (0.38–0.60)	< 0.001	0.55 (0.44–0.70)	< 0.001
eGFR < 15 mL/min/1.73m^2	0–5	533	85	1.0	–	1.0	–
	6	1,304	90	0.36 (0.26–0.48)	< 0.001	0.72 (0.53–0.97)	0.030
	7	1,844	72	0.18 (0.13–0.25)	< 0.001	0.43 (0.31–0.59)	< 0.001
	8	784	33	0.19 (0.13–0.28)	< 0.001	0.62 (0.41–0.95)	0.026
eGFR decline ≥ 30%	0–5	533	130	1.0	–	1.0	–
	6	1,304	228	0.57 (0.46–0.70)	< 0.001	0.65 (0.52–0.80)	< 0.001
	7	1,844	297	0.47 (0.38–0.58)	< 0.001	0.54 (0.44–0.67)	< 0.001
	8	784	141	0.51 (0.40–0.65)	< 0.001	0.57 (0.45–0.73)	< 0.001

Table 3. Associations of clinical quality compliance with renal events: frequency, incidence, and hazard ratios. Participants were categorized into quartiles based on their compliance to each metric. The quartiles were defined by scores of 0–5 points with n = 533 participants, 6 points with n = 1,304 participants, 7 points with n = 1,844 participants, and 8 points with n = 784 participants. Adjusted model includes adjustment for age, sex, and eGFR at the index date. *eGFR* estimated glomerular filtration rate, *HRs* Hazard ratios, *CIs* confidence intervals.

the levels of serum sodium minus chlorine (mmol/L) serve as a potential clinical biomarker for metabolic acidosis[14,18], a condition known to exacerbate renal decline. Nonetheless, it should be noted that assessing serum HCO3- beyond the simple difference between serum sodium and chloride levels would provide a more precise indication of metabolic acidosis. However, in the current study, we identified that 161 individuals (representing 3.6% of the total population) had recorded measurements of serum HCO3-. Given this, we recognized that the sample size is insufficient for robust statistical analysis of these points. Low serum calcium has been implicated in parathyroid hormone dysregulation and subsequent mineral bone disease, which could exacerbate kidney disease progression[16]. However, these associations do not imply causation. The observed electrolyte abnormalities could be a consequence of declining renal function rather than a cause. Renal impairment often leads to dysregulation of electrolyte homeostasis, and these electrolyte disturbances may serve as markers of disease severity rather than direct contributors to disease progression. Future prospective studies and clinical trials are needed to further elucidate the causative roles of these electrolyte imbalances in renal disease progression and to determine if targeted interventions can improve patient outcomes.

The observation that groups on RAS inhibitors had a higher rate of composite renal events than those not on these medications is unexpected, given the established renal protective benefits of RAS inhibitors[19–21]. Potential explanations for these findings might include the varied severity of CKD at baseline, the increased risk of hyperkalemia associated with RAS inhibitors, and potential drug interactions with RAS inhibitors. Additionally, the potential for confounding by indication should be considered. This term describes a scenario where the underlying reason for prescribing a specific treatment is directly related to the observed outcome. In this context, it is possible that patients with more progressive CKD, such as those exhibiting significant proteinuria, are more frequently prescribed RAS inhibitors. This could distort the study's results, creating an apparent association between these medications and poorer outcomes, when in reality, these drugs are being administered to patients with more severe disease presentations. A meticulous analysis that stratifies patients by CKD stage, accompanying health conditions, and proteinuria levels, while adjusting for confounding variables, is warranted to shed light on these results.

Our findings indicate that CKD patients with serum uric acid levels at or exceeding 7.0 mg/dL had higher rates of adverse renal events. This is consistent with prior studies that identifies hyperuricemia as an independent risk factor for ESRD in Japanese populations, even after adjusting for confounders such as proteinuria, hypertension, and dyslipidemia[22]. However, the literature also suggests that interventions to reduce uric acid levels may not necessarily translate to renal protection[23–25]. These may indicate that increased uric acid levels could be a marker of renal damage rather than a causative factor. It may reflect the reduced excretion by the kidneys rather than contributing directly to kidney disease progression.

The stratification of hemoglobin levels in the present study suggests a graded association with renal outcomes, where the lowest hemoglobin group (< 11 g/dL) experienced the highest rates of renal complications, followed by those within the 11–13 g/dL range, and finally the group with levels ≥ 13 g/dL. This gradation echoes the findings of earlier research[26–28]. Although prior studies suggest that anemia correction correlates with overall improved health outcomes, the direct benefit of elevating hemoglobin levels on renal outcomes remains ambiguous[29–31]. It implies that while anemia management is beneficial, there is no clear evidence that increasing hemoglobin levels beyond a certain threshold confers additional renal protection.

Our research examined the differences in the frequency of combined and specific renal events across different patient groups categorized by their CQ scores. The results indicated that patients with the lowest CQ scores, ranging from 0 to 5 points, were more likely to have a composite of renal events than those in the three higher

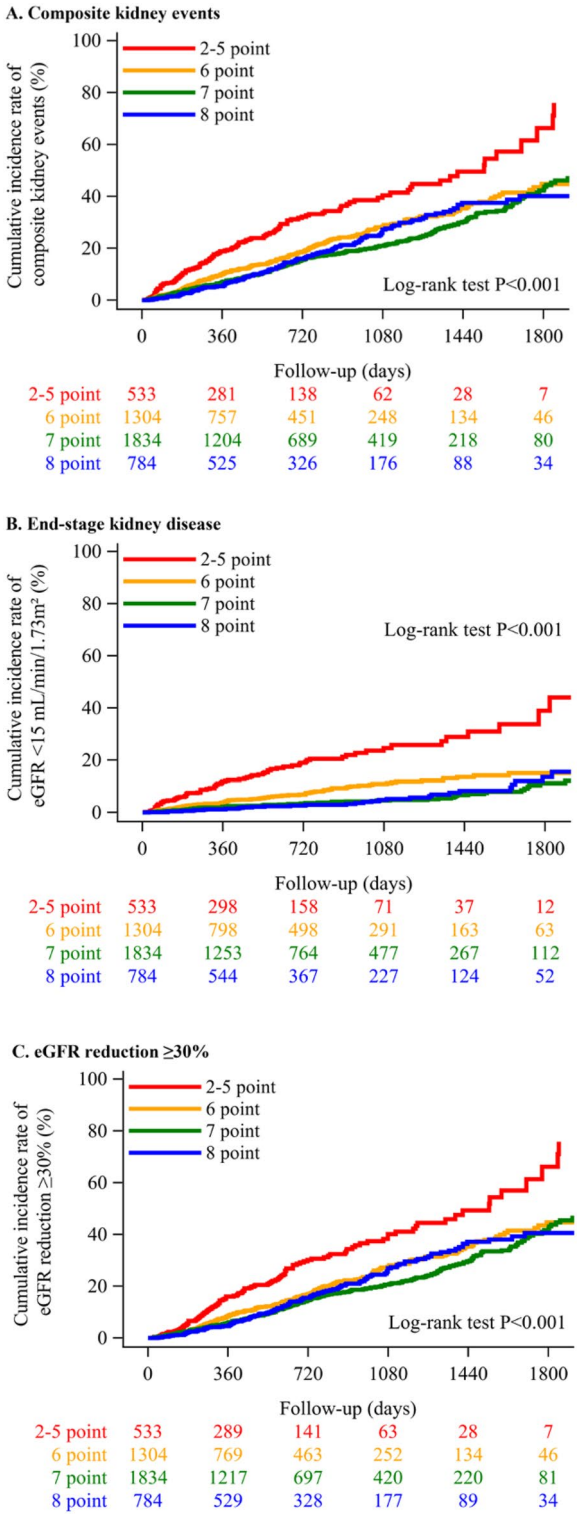

Figure 2. Cumulative incidence of composite renal events across groups based on compliance to the 2018 CKD Clinical Practice Guidelines and its associated guidelines. We defined composite renal events as either the onset of ESKD, characterized by a decline in eGFR to less than 15 mL/min/1.73 m^2, or a reduction of 30% or more in eGFR from the index date, with both conditions requiring confirmation by follow-up tests. We employed the Kaplan–Meier method to assess variations in the cumulative incidence of these renal events among quartiles, which were stratified according to compliance to the metrics set forth in the 2018 CKD Clinical Practice Guidelines and its associated guidelines. The log-rank test was then used to ascertain statistical significance, denoted by the *P*-value. CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease.

scoring brackets (6–8 points). This trend was consistent when the health outcomes were specified as either a reduction of at least 30% in the eGFR or the onset of ESKD. However, important lifestyle factors, including smoking habits and nutritional intake, and the measurements of blood pressure levels were not included in this study. These elements could significantly impact kidney function over the course of the follow-up period, and their absence in our data should be noted as a limitation. The cutoffs for categorizing using CQ scores were arbitrary that could affect the validity and applicability of the results. Determining the optimal cutoff points for CQ scores that accurately reflect patient risk categories is crucial for the reliability of the study. Furthermore, it remains uncertain whether potential synergistic effects between different CQ items were considered. Synergistic effects occur when the combined impact of two or more factors is greater than the sum of their separate effects. In the context of CKD, certain risk factors may interact in a way that significantly increases the risk of adverse renal events. Not accounting for these may oversimplify the relationships between CQ scores and health outcomes. Addressing these limitations in future research could involve developing a more robust method for determining CQ score cutoffs, analyzing the interaction between different risk factors, and ensuring that the point system reflects the relative importance of each risk factor. Additionally, a broader and more diverse patient population could help to understand the generalizability of the findings.

The current study has limitations. First, from a pool of 11,333 individuals identified as potential participants, 6,732 lacked a follow-up eGFR measurement post-index date. A possible explanation for this could be referrals to external clinics or general practitioners, as suggested by instances where patients were directed to university hospitals for evaluation of undiagnosed kidney issues. After assessments, those deemed not to require ongoing follow-up for kidney diseases within the university hospital system were referred back to their initial healthcare providers. Unfortunately, the study does not provide specific reasons for the missing follow-up eGFR data for these 6,732 patients, which limiting insight into patient care continuity. Secondly, the study faces potential selection bias. The included participants were generally younger, had lower eGFR levels, were on RAS inhibitors, and exhibited lower levels of calcium, phosphorus, and LDL cholesterol at baseline compared to those excluded. This selection of participants may affect the generalizability and interpretation of our results. Third, this dataset is derived from real-world clinical settings, where physicians determined follow-up intervals based on individual patient needs and clinical judgments. As a result, the specific intervals between eGFR measurements varied widely, which potentially affecting the generalizability and interpretation of our results. Fourth, in the current study, non-compliance among participants included both individuals receiving medication and those not receiving medication. Consequently, the potential effect of medication use on our findings was not assessed, leaving its effects uncertain.

Our study revealed that compliance to CKD guideline recommendations in clinical practice correlates with renal outcomes, underscoring the importance of guideline-concordant care, especially in a multidisciplinary fashion, in managing CKD.

Methods

The Japan Chronic Kidney Disease Database (J-CKD-DB) is a real-world electronic health record-based registry of CKD patients[32,33]. J-CKD-DB-Ex was developed based on J-CKD-DB system as a longitudinal CKD database. Data were taken from 4 university hospitals in Japan and data collection were started in January 2014, the current study is using the date followed until December 31st, 2020. This database incorporates information on inpatient and outpatient encounters, prescriptions, diagnostic codes, and laboratory measurements. The facilities participating in J-CKD-DB-Ex were required to have electronic health record systems that incorporated Standardized Structured Medical Information exchange 2 (SS-MIX2) (https://www.ss-mix.org/consE/) storage. The facilities were also required a structured data entry function that could transfer the data to the SS-MIX2 storage system[34]. With the use of SS-MIX2 storage, all data elements were extracted automatically for the avoidance of input error. After extraction, data were sent to the J-CKD-DB-Ex data center.

Fundamental standards were adopted in SS-MIX2 regarding patient profiles (the Health Level Seven [HL7] V2.5 [ISO 27931] data format), prescriptions (national drug code in Japan, HOT code), laboratory test results (Japan Laboratory Code Version 10 [JLAC10] code), diagnoses (ICD-10), and incidence of major outcomes[35–37].

This study was conducted under the oversight of the Ethical Committee of the Saitama Medical University (2022–036) and in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained through an opt-out method on the website of each participating university hospital in accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan. The inclusion criteria for the J-CKD-DB-Ex were patients aged ≥ 18 years and patients with proteinuria ≥ 1 (dipstick test), or eGFR < 60 mL/min/1.73 m^2 [32].

For the current analyses, we selected records of CKD patients leveraging the criteria of having an eGFR measurement documented on the index date (i.e., a starting point for the current study) alongside data on eight predetermined variables recorded within a six-month window preceding the index date (Fig. S1). These variables included serum potassium, serum sodium, serum chloride, serum calcium, serum phosphorus, uric acid, LDL cholesterol, and hemoglobin levels, in addition to the utilization of RAS inhibitors. The selection of these variables was grounded on the clinical advisements stipulated in the Evidence-based Clinical Practice Guidelines for CKD 2018 delineated by Japanese medical experts and by the data accessibility in the J-CKD-DB repository. We further confined our selection to CKD patient records showcasing at minimum, a single eGFR measurement transpiring after the index date.

CKD guideline component metrics

We categorized the eight component metrics derived from the Evidence-Based Clinical Practice Guidelines for CKD 2018 and its associated guidelines as follows[9–11]: (A) serum potassium (mmol/L): < 4.0, 4.0–5.4, > 5.4; (B)

serum sodium—chlorine (mmol/L): < 33, 33–36, > 36; (C) administration of RAS inhibitors (i.e., angiotensin converting enzyme inhibitors and angiotensin receptor blockers): yes or no; (D) serum calcium (mg/dL): < 8.4, 8.4–10.0, > 10.0; (E) serum phosphorus (mg/dL): < 3.5, 3.5–6.0, ≥ 6 ; (F) serum uric acid (mg/dL): < 7.0, ≥ 7.0; (G) LDL cholesterol (mg/dL): < 120, ≥ 120; (H) hemoglobin (g/dL): < 11, 11–13, > 13. Based on these categories, we developed a CQ recommendation scoring system as outlined in the Evidence-Based Clinical Practice Guidelines for CKD 2018 and its associated guidelines[9–11] (see Supplementary Table 2), assigning one point for each of the following conditions being met: (A) serum potassium ≤ 5.4 mmol/L; (B) serum sodium – chlorine ≥ 33 mmol/L; (C) administration of RAS inhibitors: yes; (D) serum calcium ≥ 8.4 mg/dL; (E) serum phosphorus reaching 6 mg/dL or higher were not detected in this cohort. Therefore, serum phosphorus < 3.5 mg/dL was defined as the reference; (F) serum uric acid < 7.0 mg/dL; (G) LDL cholesterol < 120 mg/dL; (H) hemoglobin ≥ 11 g/dL, and quantifying compliance to each metric (Table S2) on a scale from 0 (poor compliance) to 8 (full compliance).

Kidney function

Serum creatinine was assayed with an enzymatic method. eGFR was derived with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation modified by a Japanese coefficient[38]. The underlying causes of CKD were classified according to the International Classification of Diseases, Tenth Revision (ICD-10) as follows: 1) Glomerulonephritis (M321, N009, N014, N017, N019, N028-N030, N032, N033, N039); and 2) Nephrotic syndrome (N040, N042, N048, N049, N051-N055, N057, N059, N069, N083, N085). Additionally, participants were categorized based on the presence of hypertension, using ICD-10 codes I10, I110, I119, I120, I129, I139, I150-I152, I158, I159, and diabetes mellitus, identified through codes E100-E117, E119-E137, E139-E145, E148, E149, H280, H360, O240.

The primary outcome was the incidence of composite renal events across groups, classified based on their compliance to the metrics outlined in the Evidence-Based Clinical Practice Guidelines for CKD 2018[11]. We defined the composite renal evens as a persistent the onset of ESKD which was defined as an eGFR of < 15 mL/min/1.73 m^2 (confirmed by a subsequent measurement), or reduction of 30% or more in eGFR (confirmed by a subsequent measurement). In the composite end point analyses, if a participant had more than one event occur, the first event was counted as the outcome. For example, if a participant who first undergoes a reduction in eGFR of 30% or more and then, a month later, is diagnosed with ESKD, we would count only the eGFR decline of 30% or more as the outcome in the composite endpoint analysis. However, in the endpoint-specific analyses, we would count both the eGFR decline of 30% or more and the ESKD diagnosis as separate outcomes.

Statistical analysis

The descriptive statistics are presented as mean values and corresponding standard deviations, with proportions provided where relevant. We used to estimate survival functions for the Kaplan–Meier method, and compared to the differences between groups by the Log-rank test. Utilizing Cox proportional hazards regression models, we calculated HRs and their corresponding 95% CIs to assess the risk of renal events in relation to compliance or non-compliance to individual CKD guideline metrics. HRs were calculated in an unadjusted model (model 1), and after adjustments for covariates, including age, sex, and eGFR at the index date.

To determine whether the association between compliance to CKD guidelines and the incidence of composite renal events varies among the different stages of CKD, we assessed whether the association between compliance to CKD guidelines and composite renal events varies based on the participants' eGFR levels above versus below 45 mL/min/1.73 m^2 at the index date. First, we assessed we tested for heterogeneity in the association between compliance to CKD guidelines and the incidence of composite renal events by eGFR at the index date (≥ 45 mL/min/1.73 m^2 versus < 45 mL/min/1.73 m^2) with the inclusion of multiplicative interaction terms. When we identified a significant interaction ($P < 0.05$), stratified analyses according to these eGFR categories at the index date were considered. The follow-up duration was established as the time from the index date to the earliest of the following: (1) patient's departure from the medical practice or database; or (2) the final date of data collection. Statistical significance was defined as a *P* value less than 0.05 using two-sided tests using SAS version 9.4 software (SAS Institute, Cary, NC).

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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J-CKD-DB study collaborative

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ORIGINAL ARTICLE

Higher participation rates for specific health checkups are associated with a lower incidence of treated ESKD in Japan

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Abstract

Background A Japanese cohort study previously reported that not attending health checkups was associated with an increased risk of treated end-stage kidney disease (ESKD). The present study aimed to examine this association at the prefecture level.

Methods We conducted an ecological study of all prefectures in Japan ($n=47$) using five sources of nationwide open data. We explored associations of participation rates for Specific Health Checkups (SHC participation rates), the estimated prevalence of chronic kidney disease (CKD), and the ratio of nephrology specialists for each prefecture with prefecture-specific standardized incidence rates (SIRs) of treated ESKD using structural equation modeling.

Results Prefecture-specific SHC participation rates ranged from 44.2% to 65.9%, and were negatively correlated with prefecture-specific SIRs and prevalence of CKD, and positively correlated with the ratio of nephrology specialists. SHC participation rates had significant negative effects on prefecture-specific SIRs (standardized estimate (β) = − 0.38, $p=0.01$) and prefecture-specific prevalence of CKD ($\beta=-0.32$, $p=0.02$). Through SHC participation rates, the ratio of nephrology specialists had a significant indirect negative effect on prefecture-specific SIRs ($\beta=-0.14$, $p=0.02$). The model fitted the data well and explained 14% of the variance in SIRs.

Conclusions Our findings support the importance of increasing SHC participation rates at the population level and may encourage people to undergo health checkups.

Keywords Dialysis · General population · Health checkups · Regional variation · Standardized incidence ratio

Introduction

Japan, a country with one of the highest incidence and prevalence rates of treated end-stage kidney disease (ESKD) [1], has substantial regional variation in the incidence of treated ESKD [2–8] despite a uniform health care and insurance system and low ethnic and racial diversity. We previously reported associations of sex- and prefecture-specific prevalence of obesity/overweight and proteinuria with sex- and prefecture-specific standardized incidence rates (SIRs) of treated ESKD [8]. Models consisting of the prevalence of overweight/obesity, prevalence of proteinuria, and ratio of nephrology specialists explained 26% and 28% of the variance in SIRs for men and women, respectively, indicating that residual factors affect the variance in SIRs [8].

One residual factor that may affect the variance in SIRs may be participation rates for health checkups. A cohort study of Japanese adults reported that not attending health checkups was associated with an increased risk of treated ESKD, defined as the initiation of kidney replacement therapy with hemodialysis, peritoneal dialysis, or kidney transplantation [9]. Thus, prefectures with low participation rates for health checkups may have an increased incidence of treated ESKD. In fact, large variations have been observed by prefecture in participation rates for Specific Health Checkups (hereafter, SHC participation rates), an annual health screening program introduced by Japan's Ministry of Health, Labour and Welfare since 2008 to identify individuals requiring specific health guidance for the purpose of reducing the number of people having, or at risk for, metabolic syndrome [10]. The SHC participation rate in 2008

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was 38.5% and varied widely by prefecture, ranging from 27.5% to 53.3% (Supplementary Table 1).

To date, however, no study has examined the association between SHC participation rates and the incidence of treated ESKD at the prefecture level. Accordingly, this ecological study aimed to examine the relationship between prefecture-specific SHC participation rates and SIRs of treated ESKD in Japan. We also evaluated the prevalence of chronic kidney disease (CKD) in each prefecture as a potential mediator between SHC participation rates and SIRs of treated ESKD, as well as the ratio of nephrology specialists to all physicians in each prefecture as a surrogate indicator for the quality of CKD care. We tested the hypothesis that regional variation in the incidence of treated ESKD among the general Japanese population could be explained, at least in part, by prefecture-specific SHC participation rates.

Materials and methods

Study design and data source

This cross-sectional ecological study used data from five sources of nationwide open data: Data on SHC and Specific Health Guidance [10], the annual survey of the Japanese Society for Dialysis Therapy Renal Data Registry (JRDR), national vital statistics, National Database of Health Insurance Claims and SHC of Japan (NDB) Open Data, and Statistics of Physicians, Dentists and Pharmacists. SHC participation rates in 2019 of each prefecture were extracted from the Data on SHC and Specific Health Guidance [10] reported by the Ministry of Health, Labour and Welfare.

An incident case of treated ESKD was defined as a patient with loss of kidney function that resulted in maintenance dialysis therapy including both hemodialysis and peritoneal dialysis [11]. Given the small number of pre-emptive kidney transplant patients in Japan [12], this definition covers almost all treated ESKD patients in Japan. Incident cases of treated ESKD were extracted from annual data of the JRDR for 2020 and 2021 using the Web-based Analysis of Dialysis Data Archives (WADDA) system [13]. Details on registry data collection techniques and characteristics of this dialysis population have been described elsewhere [13, 14]. In brief, the JRDR collects data every year through questionnaire surveys sent to all dialysis facilities in Japan. The population for each prefecture during the same 2-year period was obtained from national vital statistics. SIR of treated ESKD was calculated as the ratio of the observed number of incident cases of treated ESKD patients to the expected number of incident cases of treated ESKD using the indirect method previously described [8, 15].

Numbers of people aged 40–74 years stratified by eGFR and proteinuria levels in each prefecture for 2019 were obtained from NDB Open Data [16]. Details of NDB Open Data have been described elsewhere [17]. In brief, NDB, a large national administrative claims database, refers to the National Database of Health Insurance Claims and SHC of Japan operated by the Ministry of Health, Labour and Welfare. NDB Open Data were constructed by aggregating a part of NDB without any confidential information [17]; therefore, researchers using NDB Open Data cannot access patient- or facility-level information.

The prefecture-specific prevalence of CKD was calculated as the estimated number of people aged 40–74 years with CKD divided by the total number of people aged 40–74 years in each prefecture. CKD was defined as an eGFR < 60 mL/min/1.73 m^2 and/or proteinuria [18]. Proteinuria was defined as a dipstick urinalysis score of 1 + or greater (equivalent to ≥ 30 mg/dL). The number of people aged 40–74 years with CKD in each prefecture was estimated as follows. First, we calculated the prevalence of CKD by 5-year age bands and sex in each prefecture using data obtained from NDB Open Data [16] by dividing the number of participants with CKD by the total number of SHC participants. Next, we estimated the number of people with CKD by 5-year age bands and sex by multiplying the prevalence of CKD with the corresponding age- and sex-specific number of people in the general population in each prefecture, assuming that the prefecture-specific prevalence of CKD among participants in NDB Open Data is the same as that of the entire population. We then summed the number of people with CKD aged 40–74 years in each prefecture, and estimated the prefecture-specific prevalence of CKD by dividing the estimated number of people aged 40–74 years with CKD by the total number of people aged 40–74 years in each prefecture. Similarly, we estimated the number and prevalence of prefecture-specific CKD patients aged 60–74 years.

Numbers of nephrology specialists and all physicians in each prefecture were extracted from the Statistics of Physicians, Dentists and Pharmacists reported by the Ministry of Health, Labour and Welfare [19]. We used data from 2020 since the statistics are reported every two years. The prefecture-specific ratio of nephrology specialists to all physicians was calculated as the number of nephrology specialists divided by the total number of all physicians by prefecture.

The present study was conducted according to the principles of the Declaration of Helsinki. All data used in the analyses were anonymized and included no individual patient data. Thus, ethical review and informed consent were not required.

Statistical analysis

Pearson's correlation coefficients were used to evaluate relationships between variables. Hierarchical multiple

regression was used to clarify further the comparative effects of prefecture-specific SHC participation rates, prefecture-specific prevalence of CKD, and prefecture-specific ratio of nephrology specialists on prefecture-specific SIRs. In Model 1, prefecture-specific SHC participation rates were first entered into the regression model as an independent variable. In Model 2, prefecture-specific prevalence of CKD was added. In Model 3, prefecture-specific ratio of nephrology specialists was added. Adjusted R-squared values were used to determine the percentage of variation explained by the independent variable(s) that affects the dependent variables. Multicollinearity of independent variables was assessed by variation inflation factor (VIF). A VIF of 10 is considered excessive, while a VIF as low as 4 indicates high levels of multicollinearity between predictor variables.

Structural equation modeling (SEM) was performed to evaluate the impact of the association between SHC participation rates, prevalence of CKD, and ratio of nephrology specialists on prefecture-specific SIRs. We developed a model for SIR that included variables based on results of the correlation analysis. Direct effects are shown as arrows originating from an independent variable leading and pointing to a dependent variable. Indirect effects are shown as a mediating variable with an arrow pointing to it from an independent variable and also an arrow pointing to another dependent variable. Indicators to evaluate goodness-of-fit of the structural equation model included the chi-square statistic, Comparative Fit Index (CFI), adjusted Goodness-of-Fit Index (AGFI), and Root Mean Square Error of Approximation (RMSEA). Our goals for model fit were: non-significant chi-square statistic, CFI > 0.90, AGFI > 0.90, and RMSEA < 0.08 [20].

All reported *P*-values were two-sided, and $P < 0.05$ was considered statistically significant. Statistical analyses were performed using AMOS version 27 (IBM Inc, Armonok, NY) and IBM SPSS Statistics version 27 (SPSS, Chicago).

Results

The national SHC participation rate was 55.3% in 2019 (Supplementary Table 2). SHC participation rates varied widely by prefecture, ranging from 44.2% to 65.9%. Prefecture-specific SHC participation rates in 2019 were highly correlated with those in 2008 ($R^2 = 0.81$, $p < 0.001$). Prefecture-specific SIRs also varied by prefecture, ranging from 0.73 to 1.34. In 2019, 9,420,443 adults aged 40–74 years were estimated to have CKD, which accounted for 16% of people aged 40–74 years in Japan. The estimated prevalence of CKD among people aged 40–74 years varied by prefecture, ranging from 11 to 20%. The estimated prevalence of CKD among people aged 60–74 years was 25% in Japan and also varied by prefecture, ranging from 16 to 30% (Supplementary Table 3). The prefecture-specific CKD prevalence among people aged 40–74 years was highly correlated with that among people aged 60–74 years ($R^2 = 0.83$, $p < 0.001$). In 2020, 323,700 medical doctors worked at medical facilities in Japan, and of these, 5,360 (1.7%) were nephrology specialists. The ratio of nephrology specialists ranged from 0.2% to 2.3%.

Figure 1 shows prefecture-specific SHC participation rates in ascending order. Prefectures with high participation rates were more likely to have lower SIRs for treated ESKD than the national average (i.e., 1.0), a lower prevalence of CKD than the national prevalence (i.e., 16%), and a higher ratio of nephrology specialists than the national ratio (i.e., 1.7%).

Pearson's correlation analysis revealed that SHC participation rates were negatively correlated with both prefecture-specific SIRs ($r = -0.34$, $p = 0.02$) and prevalence of CKD ($r = -0.32$, $p = 0.03$), but positively correlated with the ratio of nephrology specialists ($r = 0.36$, $p = 0.01$) (Table 1). No significant correlations were observed between prefecture-specific SIRs, prevalence of CKD, and ratios of nephrology specialists (Supplementary Figure). Furthermore, no significant association was observed between the prefecture-specific prevalence of CKD among people aged 60–74 years and prefecture-specific SIRs ($r = 0.24$, $p = 0.11$).

Hierarchical linear regression analysis revealed that SHC participation rates were significantly and negatively associated with prefecture-specific SIRs (Table 2). Further adjusting for the prevalence of CKD (Model 2) and ratio of nephrology specialists (Model 3) did not change the association between SHC participation rates and prefecture-specific SIRs.

Based on these results, a hypothetical model was constructed (Fig. 2). SHC participation rates had a significant total effect on prefecture-specific SIRs ($\beta = -0.38$, $p = 0.01$), which was the sum of a direct negative effect on prefecture-specific SIRs ($\beta = -0.33$, $p = 0.03$) and an indirect negative effect through the prefecture-specific prevalence of CKD ($\beta = -0.04$, $p = 0.33$) (Table 3). SHC participation rates also had a significant direct negative effect on the prefecture-specific prevalence of CKD ($\beta = -0.32$, $p = 0.02$). The direct path from the prefecture-specific prevalence of CKD to prefecture-specific SIRs, however, was not significant ($\beta = 0.13$, $p = 0.36$). The ratio of nephrology specialists had a significant indirect negative effect through SHC participation rates ($\beta = -0.14$, $p = 0.02$) and a non-significant direct positive effect on prefecture-specific SIRs ($\beta = 0.10$, $p = 0.51$), resulting in a non-significant total effect on prefecture-specific SIRs ($\beta = -0.04$, $p = 0.71$). The fit of the model to the data was excellent (chi-square value = 0.13, df = 1, $p = 0.72$, CFI = 1.00, AGFI = 0.99, and RMSEA = 0.00), and this model explained 14% of the variance in prefecture-specific

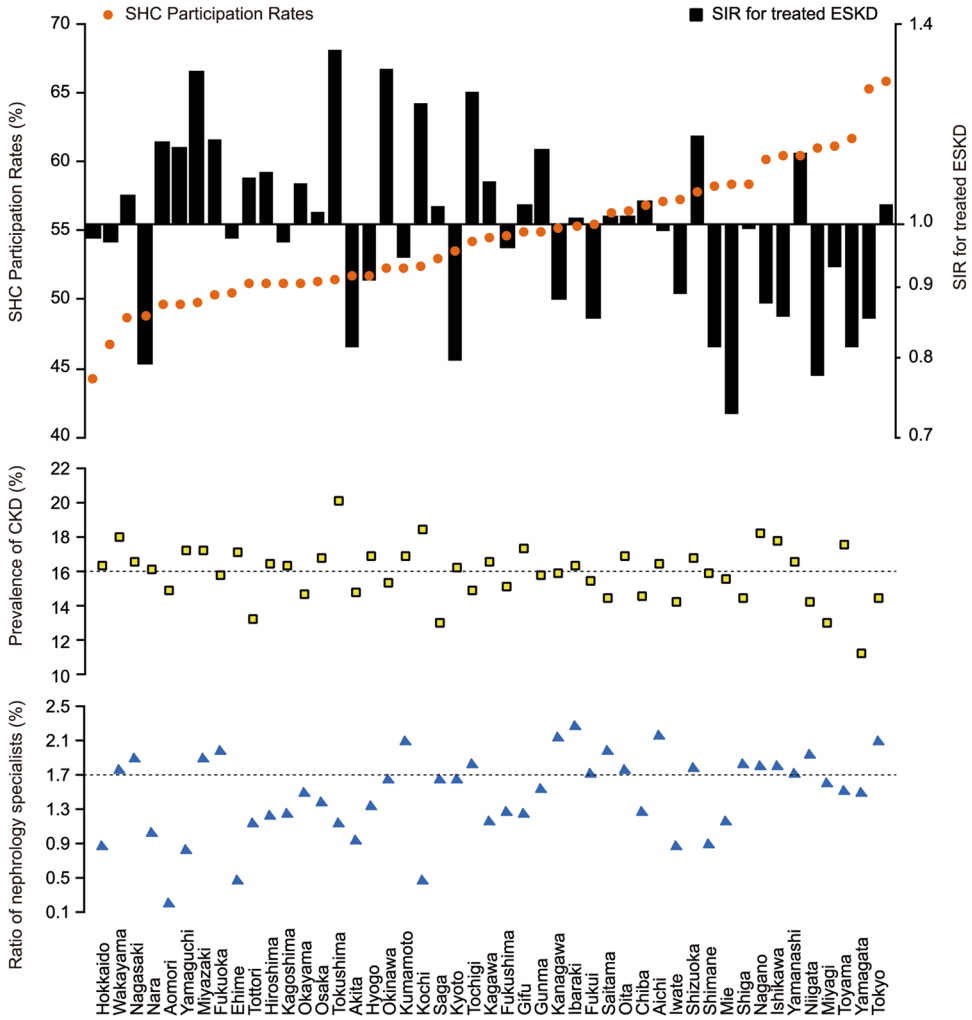

Fig. 1 SHC participation rates, SIRs of treated ESKD, prevalence of CKD, and ratio of nephrology specialists in the 47 prefectures. Prefecture-specific SIRs are presented in ascending order. Note that the y-axis in SIR for treated ESKD is a logarithmic scale. Dashed lines show national averages. *CKD* chronic kidney disease, *ESKD* end-stage kidney disease, *SHC* specific health checkups, *SIR* standardized incidence ratio

Table 1 Pearson correlation analysis between variables

Variables	SHC participation rates	SIR for treated ESKD	Prevalence of CKD	Ratio of nephrology specialists
SHC participation rates	1			
SIR for treated ESKD	− 0.34 0.02	1		
Prevalence of CKD	− 0.32 0.03	0.23 0.12	1	
Ratio of nephrology specialists	0.36 0.01	− 0.03 0.82	− 0.07 0.64	1

The upper value is the linear correlation coefficient and the lower value is the *p*-value

CKD chronic kidney disease, *ESKD* end-stage kidney disease, *SHC* Specific Health Checkups, *SIR* standardized incidence ratio

SIRs. When using the prefecture-specific prevalence of CKD among people aged 60–74 years instead of that among people aged 40–74 years, the fit of the SEM model to the data was poor (chi-square value = 2.129, df = 1, $p = 0.14$, CFI = 0.91, AGFI = 0.78, RMSEA = 0.16).

Discussion

This ecological study using SEM revealed that SHC participation rates had significant direct negative effects on

Table 2 Hierarchical regression analysis for variables predicting SIRs

Variables	Model 1		Model 2		Model 3	
	β	*P*	*β*	*P*	*β*	*P*
SHC participation rates	− 0.34	0.02	− 0.30	0.05	− 0.33	0.04
Prevalence of CKD			0.14	0.36	0.13	0.38
Ratio of nephrology specialists					0.10	0.53
Adjusted R^2	0.10		0.09		0.08	
F for change in R^2	5.94	0.02	0.85	0.36	0.40	0.53

N for all variables = 47

*β*standardized regression coefficient, *CKD* chronic kidney disease, *SHC* specific health checkups, *SIR* standardized incidence ratio

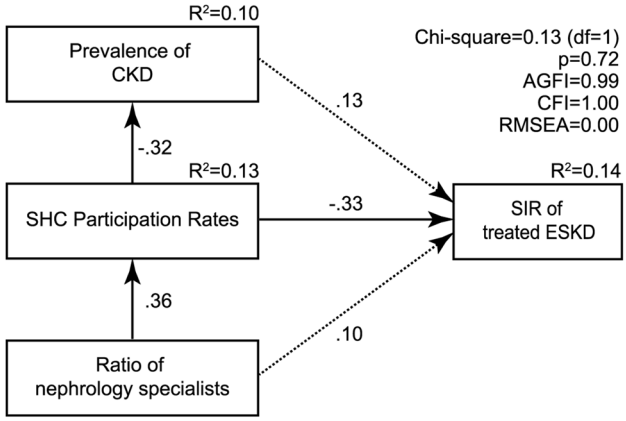

Fig. 2 SEM models and standardized estimates. Solid lines indicate significant paths. Dashed lines indicate non-significant paths. The standardized regression coefficient is provided for each relationship. For simplicity, residual variance associated with independent variables is not represented. *CKD* chronic kidney disease, *ESKD* end-stage kidney disease, *SEM* structural equation modelling, *SIR* standardized incidence ratio

Table 3 Structural equation modeling: standardized direct, indirect, and total effects

Paths	β	*P*
SHC participation rates → SIR of treated ESKD		
Standardized direct effect	− 0.33	0.03
Standardized indirect effect	− 0.04	0.33
Standardized total effect	− 0.38	0.01
Ratio of nephrology specialists → SIR of treated ESKD		
Standardized direct effect	0.10	0.51
Standardized indirect effect	− 0.14	0.02
Standardized total effect	− 0.04	0.71

N for all variables = 47

*β*standardized regression coefficient, *ESKD* end-stage kidney disease, *SHC* specific health checkups, *SIR* standardized incidence ratio

prefecture-specific SIRs and prefecture-specific prevalence of CKD. Furthermore, through SHC participation rates, the ratio of nephrology specialists had a significant indirect negative effect on prefecture-specific SIRs, suggesting that a higher prefecture-specific ratio of nephrology specialists was associated with lower prefecture-specific SIRs. The SEM model explained 14% of the variance in prefecture-specific SIRs, indicating that prefecture-specific SHC participation rates can partially explain regional variation in prefecture-specific SIRs of treated ESKD.

SHC participation rates had a significant impact on prefecture-specific SIRs and prevalence of CKD, suggesting that increasing SHC participation rates could potentially have a preventive effect on CKD and ESKD in the general population. This is in line with the Neyagawa Health checkups and Health care in Kokuho database (NHHK) study, which showed that men who did not attend health checkups and did not undergo a kidney test using dipstick urinalysis and/or serum creatinine measurement at medical facilities were at significantly higher risk of treated ESKD than those who attended checkups, especially among those aged ≥ 75 years [9]. Although SHCs focus on metabolic syndrome rather than CKD, preventing metabolic syndrome could reduce the likelihood of developing CKD and ESKD. A recent review of randomized controlled trials and observational studies reported that general health checks were associated with increased chronic disease recognition and treatment, risk factor control, preventive service uptake, and improved patient-reported outcomes [21]. The review reported that general health checks were sometimes associated with modest improvements in health behaviors, such as physical activity and diet [21]. Health behaviors are significantly associated with incident diabetes, hypertension, and CKD in the general population [22–24]. These reports and our present findings, taken together, suggest the possibility that increasing SHC participation rates can reduce the incidence of treated ESKD.

Although SHC participation rates had a significant direct negative effect on the prefecture-specific prevalence of CKD, the path from prevalence of CKD to prefecture-specific SIRs

was not significant. This may be because the prevalence of CKD was estimated among people aged 40–74 years who participated in SHCs, which may not be the same as that of the general population in each prefecture. Although we assumed that the prefecture-specific prevalence of CKD among participants in NDB Open Data is the same as that of the entire population, this may not be the case. According to the NHHK study, men who did not attend health checkups were at significantly higher risk of treated ESKD than those who attended checkups [9], suggesting that the prevalence of CKD among SHC participants would be lower than that among non-participants. If this is true, our calculations may have underestimated the prevalence of CKD and this may explain why the path from the prevalence of CKD to prefecture-specific SIRs was not significant.

We found that the ratio of nephrology specialists had a significant indirect path to prefecture-specific SIRs through SHC participation rates, indicating that a higher prefecture-specific ratio of nephrology specialists was associated with lower prefecture-specific SIRs via increased SHC participation rates. This could be explained by measures against CKD taken by the Japanese government starting in 2008 and recently updated in 2018 [25]. Since one of the aims of the measures is to prevent CKD exacerbation through early detection and diagnosis of CKD, prefectures with a high ratio of nephrology specialists may be more active in encouraging people to undergo health checkups to prevent both CKD and ESKD.

The national SHC participation rate increased from 38.5% in 2008 to 55.3% in 2019, although large variations were observed by prefecture in 2019, ranging from 44.2% to 65.9%. Prefecture-specific SHC participation rates in 2019 were highly correlated with those in 2008, suggesting that maintaining high SHC participation rates for years may be associated with a decreased incidence of treated ESKD and a decreased prevalence of CKD.

This study has several strengths. First, since data were extracted from nationwide sources, our findings are broadly generalizable to the Japanese population. Second, to the best of our knowledge, this is the first study to report associations of prefecture-specific SHC participation rates with prefecture-specific SIRs of treated ESKD. Our findings provide evidence that low SHC participation rates are associated with a high incidence of treated ESKD from a population-level perspective.

There are also several limitations worth noting. First, although we targeted all 47 prefectures in Japan ($n=47$), we could only use a limited number of parameters to estimate SEM models. Second, only patients who had undergone dialysis treatment were included, as data were not available for patients who had not initiated dialysis or had undergone preemptive kidney transplantation in Japan. The number of preemptive kidney transplants in Japan, however, is small, with only 662 patients being reported in 2017 [12]. In addition, data were unavailable for patients with ESKD who did not receive renal replacement therapy. Third, we assumed that the prefecture-specific prevalence of CKD among participants in NDB Open Data is the same as that of the entire population. However, no data were available about the prevalence of CKD among non-participants. Finally, since this was an ecological study, there is a risk of ecological fallacy, i.e., findings observed at the prefecture level may not be seen at the individual level. However, the NHHK study showed that not attending health checkups was associated with an increased risk of ESKD even at the individual level [9], suggesting that increasing SHC participation rates is important for preventing ESKD at both the individual and prefecture levels.

Conclusions

This ecological study showed that higher prefecture-specific SHC participation rates are associated with lower prefecture-specific SIRs of treated ESKD. Our findings provide evidence to support the importance of increasing SHC participation rates from a population-level perspective and may encourage people to undergo health checkups.

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Declarations

Conflict of interest The authors declare that no conflict of interest exists.

Research involving human participants and/or animals This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Obtaining consent was not required because the current analyses used existing national data without any individual patient data.

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原　著

近年の透析導入率の変化，2006～2021年

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Updated trends in incidence rates of dialysis in Japan, 2006-2021

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要　旨

目　的：2018年に腎疾患対策検討会報告書(以下，報告書)が発出され，達成すべき成果目標(key performance indicator：KPI)の一つとして，2028年までに年間新規透析導入患者数を3万5千人以下に減少させることが掲げられた。そこで，2021年までの透析導入率の経年変化を評価し，報告書発出後の4年間で透析導入率の低下により透析導入を防げたと考えられる人数，そして透析導入率が変化しない場合に予測される透析導入患者数を推計した。

方　法：2006～2021年の日本透析医学会統計調査，人口統計を用いて，性年齢階級別に透析導入率を算出した。透析導入率が報告書の発出前2年間(2016～2017年)の平均のまま不変と仮定した場合，予測される透析導入数をその後の4年間(2018～2021年)の各年人口から求め，実際の導入数との差を求め，透析導入率低下により透析導入を防げたと考えられる人数を推計した。将来推計人口を用いて，2021年の透析導入率のまま不変であった場合に，予測される2025年ならびに2030年の透析導入患者数を推計した。

結　果：性年齢階級別透析導入率のグラフは，年々，全体的に高齢の方へシフトしており，透析導入が先送りされていることが示唆された。報告書発出後の4年間で，透析導入率の低下により3,725人の透析導入を防ぐことができたと推計された。透析導入率が現状のままなら，透析導入患者数は2025年39,319人，2030年40,213人と，目標の3万5千人以下には達しないことが推計された。

総　括：報告書発出後も透析導入率は低下しており，対策の効果と考えられた。しかし，現状(2021年時点)での透析導入率のままでは，KPIは達成されないと推計され，目標達成のためには，透析導入率をさらに下げることが必要である。

Background：Since 2018, the Japanese government has started new measures against chronic kidney disease (CKD). This study aimed to examine trends in the sex- and age-specific incidence rates of dialysis between 2006 and 2021 and assess the impact of population aging on the number of incident dialysis patients over the next decade in Japan.

Methods：Incidence was calculated using published data and Japan's population statistics. The 2021 incidence was extrapolated, and projected future demographic changes within the Japanese population were used to estimate the

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number of incident dialysis patients in 2025 and 2030.
Results：The sex- and age-specific incidence rates of dialysis decreased gradually between 2006 and 2021, except among males aged ≥ 80 years. The total number of incident dialysis patients was projected to increase from 37,968 in 2021 to 39,319 in 2025 and 40,213 in 2030, under the assumption that age- and sex-specific incidence rates observed in 2021 will remain constant over the next decade.
Conclusions：This study shows that the number of patients who initiate dialysis treatment is projected to increase over the next decade in Japan due to the aging of the population. The incidence rates significantly decreased after the reference year of 2018, suggesting that the new measures against CKD significantly prevented the progression of this disease. However, the total number of incident dialysis patients was projected to increase in 2025 and 2030. Our findings suggest the need to decrease age- and sex-specific incidence rates below the current level.
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Key words：chronic kidney disease, dialysis, incidence, trend

はじめに

日本は，人口あたりの腎代替療法を要する末期腎不全患者数が，2020年の報告で台湾，韓国に次いで世界で3番目に多く[1]，その発症率は台湾，米国，シンガポール，韓国，タイに次いで世界で6番目に高いなど[1]，腎疾患は国民の健康に重大な影響を及ぼしている。さらなる腎疾患対策の推進のため，2018年7月に「腎疾患対策検討会報告書～腎疾患対策のさらなる推進を目指して～」[2,3]（以下，報告書と略す）が取りまとめられた。その中で，達成すべき成果目標（key performance indicator：KPI）の一つとして，2028年までに，年間新規透析導入患者数を3万5,000人以下に減少させることが設定された[2～4]。

われわれは，1983年から2016年までの日本透析医学会統計調査と人口統計を用いて，わが国の透析導入率は高齢男性を除き，近年，低下傾向にあることを報告した[5]。2018年に報告書[2]が発出され，本報告書に基づく腎疾患対策が全国で展開されていることから，さらに透析導入率が低下していることが考えられる。

そこで，報告書発出後の中間評価として，2021年までの透析導入率の経年変化を評価した。透析導入率の変化を具体的な人数で表現するため，腎疾患対策検討会報告書の発出前のまま透析導入率が不変であった場合，性年齢階級別人口から予測される透析導入数を計算し，実際の導入数との差を求め，透析導入率低下により透析導入を防ぐことができたと考えられる人数を算出した。そして，現状（2021年）の透析導入率のまま不変であった場合，将来推計人口から予測される予測透析導入患者数を推計した。

対象と方法

1. データ

解析対象者は2006年～2021年の新規導入患者とし，同年の日本透析医学会統計調査，人口統計，将来推計人口（令和5年推計）を用いた。データは，日本透析医学会の会員ホームページからアクセス可能なWeb-based Analysis of Dialysis Data Archives（WADDA）システム[6]，政府統計の総合窓口（e-Stat）[7,8]，および，国立社会保障・人口問題研究所のホームページ[9]から入手した。

WADDAシステムは，利用者がパラメータ指定することで随意の帳票出力が可能である。人数のみの情報が得られ，個人情報は含まれない。本分析では，以下の出力帳票を用いた。

調査年：2006年～2021年患者，集計対象：新規導入患者（年末死亡，離脱，移植含む）

縦軸：年齢（調査年末時），横軸：性別

倫理的配慮：本解析は，個人情報を含まない公表されている集計数字を用いた解析であり，人を対象とする生命科学・医学系研究に関する倫理指針（令和3年3月23日，令和4年3月10日一部改正，文部科学省，厚生労働省，経済産業省）の適用外である。

2. 計算方法

透析導入患者の高齢化を表現するため，年末調査時に80歳以上，あるいは85歳以上の透析導入患者数を全導入数で割り，そのパーセンテージを男女別に求めた。

性年齢階級別透析導入率を以前に報告した方法[10～12]で計算した。すなわち，性年齢階級別透析導入患者数を分子に，分母を性年齢階級別人口として求め，人口千人あたりで表現した。

$$性年齢階級別透析導入率=\frac{性年齢階級別透析導入患者数}{性年齢階級別人口}$$

経年変化を視覚的にわかりやすくするため，2006 年から 2021 年までの 16 年間を，単年毎のグラフに加えて，4 年毎（2006〜2009，2010〜2013，2014〜2017，2018〜2021）にまとめた形でもグラフ化した。

$$4\text{年毎の性年齢階級別透析導入率}=\frac{4\text{年間の性年齢階級別透析導入患者数}}{4\text{年間の性年齢階級別人口}}$$

報告書発出後の変化を具体的な人数で表現するため，報告書発出前 2 年間（2016〜2017 年）の透析導入率の平均を性年齢階級別に求め，この透析導入率のまま不変であった場合に，各年の人口から予測される透析導入数を下記の式を用いて報告書発出後の 4 年間（2018〜2021 年）で計算した。

$$予測透析導入患者数=\sum(性年齢階級別透析導入率\times性年齢階級別人口)$$

この予測数と実際の透析導入数との差を求めることで，透析導入率の低下により，この 4 年間に何人の透析導入を防げたと考えられるかが表現される。各年毎，性年齢階級別にも，予測透析導入数と実際の透析導入数の差を求めた。

2025 年と 2030 年の将来推計人口（令和 5 年推計）と 2021 年の性年齢階級別透析導入率を用いて，上記の予測透析導入患者数を求める式で，透析導入率が現状のまま不変であった場合，2025 年と 2030 年に予測される透析導入患者数を計算した。そして，高齢化を評価するため，80 歳以上，85 歳以上で導入される患者割合を予測数から計算した。

最後に，どのくらい透析導入率を下げれば，KPI が達成されるのかの目安にするため，2020 〜 2021 年の全国透析導入率を 100％とした場合，性年齢を調整した標準化透析導入比が 95％である熊本県[13]の性年齢階級別透析導入率を用いて，上記と同様に，将来推計人口から予測される透析導入患者数を 2025 年と 2030 年で計算した。

結　果

2021 年の透析導入患者数は，患者調査票で 37,968 人（男性 26,325 人，女性 11,643 人），うち 7 人の年齢が不明であった[14]。この人数は，報告書発出前の 2016 年（37,250 人）[15]と 2017 年（38,786 人）[16]の平均（38,018 人）よりも 50 人少なかった。透析導入患者の平均年齢は 71.09 歳（男性 70.38 歳，女性 72.21 歳）と，2016 年（69.40 歳）[15]，2017 年（69.68 歳）[16]と比べ，年々，高齢化していた。

2021 年の透析導入患者のうち，年末調査時の年齢が 80 歳以上の割合は，男性 27％（7,204 人），女性 37％（4,288 人），85 歳以上の割合は，男性 13％（3,307 人），女性 19％（2,176 人）であった。言い換えると男性導入患者の約 4 人に 1 人，女性導入患者の約 3 人に 1 人が 80 歳以上での透析導入であり，男性導入患者の約 8 人に 1 人，女性導入患者の約 5 人に 1 人は 85 歳以上での透析導入であった。

2006 年から 2021 年までの性年齢階級別透析導入率は，黒で示した 2018 年（報告書発出年）以降，男女とも 80 歳未満では低下傾向にあった（**Fig.1**）。

4 年間毎にまとめた経年変化（**Fig.2**）では，年々，グラフが全体的に右（高齢）方へシフトしていることが見て取れ，透析導入を先送りできていることが示唆された。黒色の線で示したグラフは，直近の 4 年間（2018〜2021 年）の透析導入率であり，報告書発出以後に相当する。80 歳以上の年齢階級では，男性では直近の 4 年間は透析導入率が上昇していたが，女性では低下傾向にあった。

透析導入率の変化を具体的な人数で表現するため，報告書発出前 2 年間（2016〜2017）の透析導入率のまま不変であった場合，各年の性年齢階級別人口から予測される透析導入数を 2018〜2021 年で計算し，実際の導入数との差を求めた（**Table 1**）。4 年間を合計した結果，予測導入患者数は，156,946 人と求められ，実導入数（153,221 人）との差は，3,725 人となった。年齢階級別にみると，男性は 74 歳以下，女性は 84 歳以下でその差は正，すなわち，予測数よりも実数が下回っていた。一方，それよりも高齢の男性および 85-〜94 歳の女性では，その差が負，すなわち予測数よりも実数が上回っていた。

各年毎に予測数と実数の差を計算すると，2018 年は 555 人（予測導入患者数 38,702 人の 1.4％に相当），2019 年は 560 人（予測導入患者数 39,118 人の 1.4％に相当），2020 年は 898 人（予測導入患者数 39,447 人の 2.3％に相当），2021 年は 1,712 人（予測導入患者数 39,680 人の 4.3％に相当）と，年々，その差は大きくなり，予測数に占める割合も大きくなっていることが確認された（**Table 2**）。

仮に，透析導入率が現状（2021 年）のままなら，将来推計人口（令和 5 年推計）から計算された透析導入患者数は 2025 年 39,319 人（男性 27,282 人，女性 12,037 人），2030 年 40,213 人（男性 27,918 人，女性 12,295 人）と推計され（**Table 3**，**Fig.3**），目標の 3 万 5 千人以下は達成されないことが示唆された。透析導入患者のうち 80 歳以上の割合は，2025

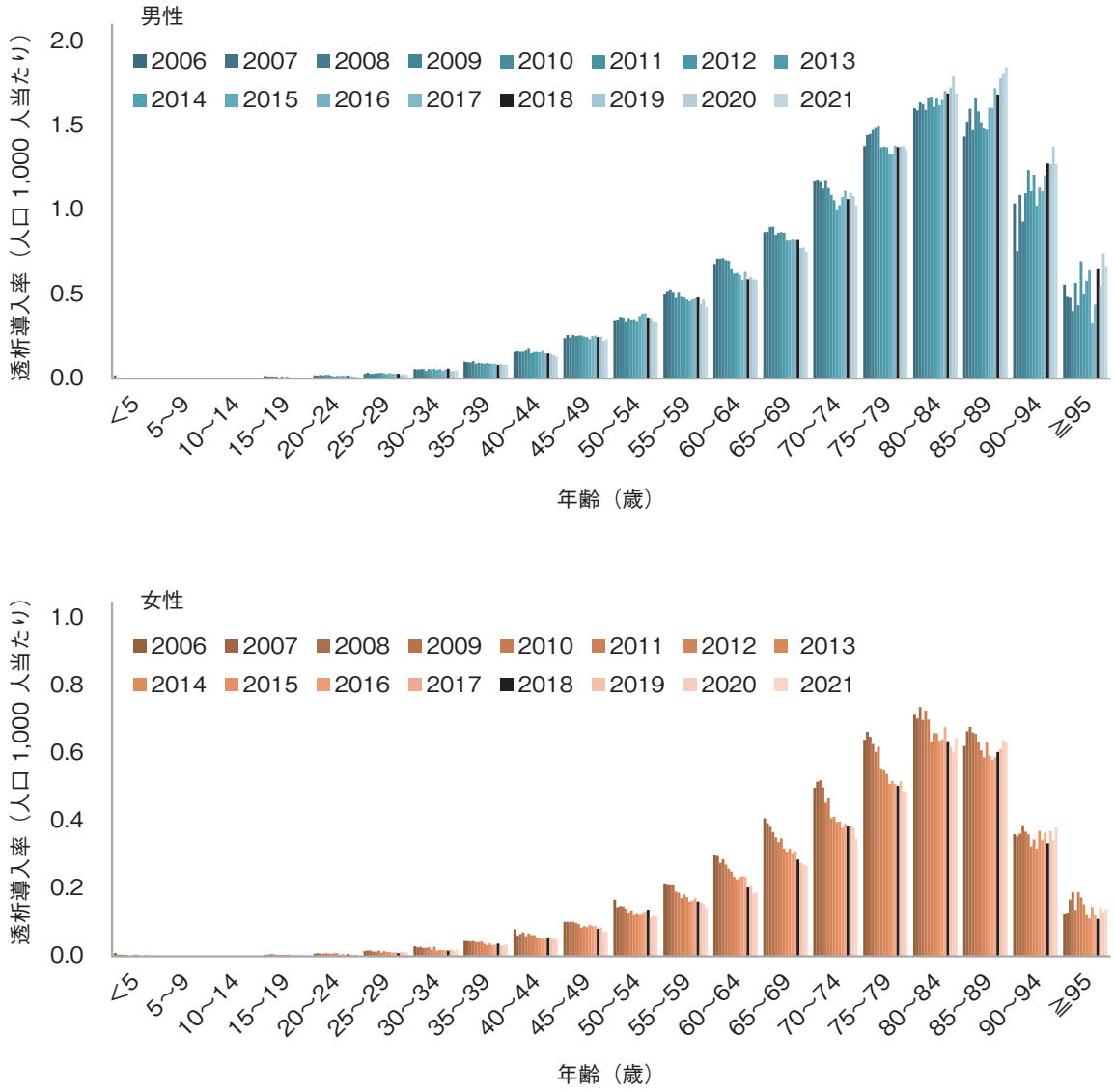

Fig. 1　男女別・年齢階級別透析導入率の経年変化（2006 ～ 2021 年）
黒色のバーは，報告書が発出された 2018 年の透析導入率を示す。

年は男性 29%（8,011 人），女性 39%（4,667 人），2030 年は男性 35%（9,694 人），女性 44%（5,418 人）と，男性導入患者の約 3 人に 1 人，女性導入患者の約 2 人に 1 人が 80 歳以上での透析導入になると推計された。同様に，透析導入患者のうち 85 歳以上の割合は，2025 年は男性 14%（3,752 人），女性 20%（2,376 人），2030 年は男性 16%（4,409 人），女性 22%（2,698 人）と，男性導入患者の約 6 人に 1 人，女性導入患者の約 5 人に 1 人が 85 歳以上での透析導入になることが推計された。

仮に，全国の透析導入率を現状（2021 年）の全国透析導入率よりも 5%低い熊本県のレベルまで下げることができれば，将来推計人口から予測される透析導入患者数は 2025 年 33,096 人（男性 24,338 人，女性 8,758 人），2030 年 33,435 人（男性 24,645 人，女性 8,790 人）となり，目標の 3 万 5 千人以下が達成されることが推計された。

考　察

本研究は，透析導入率の経年変化を評価し，以下の点を明らかにした。①男女とも透析導入率のグラフは年々，右（高齢）方へシフトしており，透析導入を先送りできているが，80 歳以上の男性では透析導入率が以前よりも上昇している，②報告書発出後の 4 年間で，透析導入率の低下により 3,725 人の透析導入を防ぐことができたと推計される，

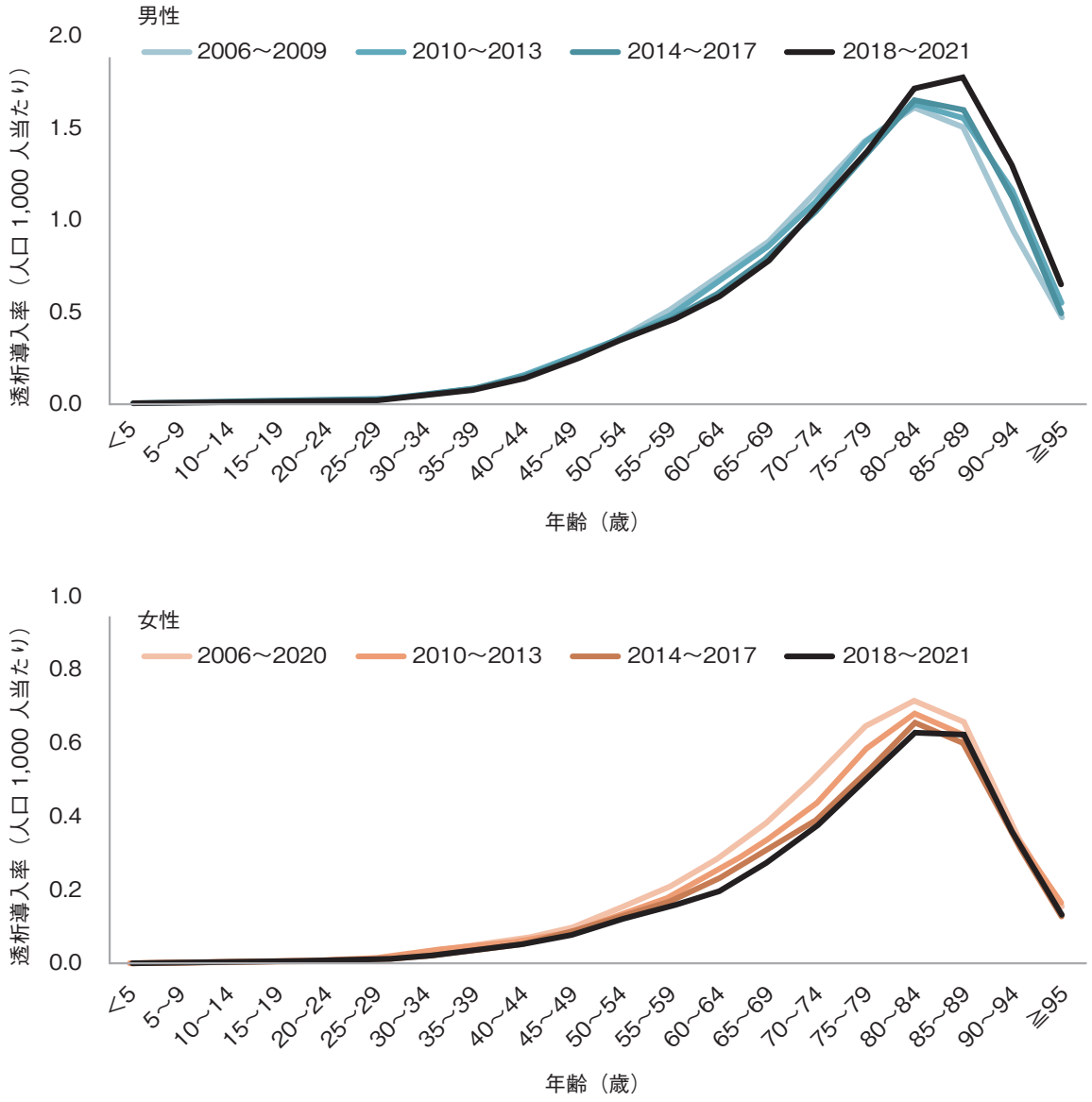

Fig 2　4 年毎の男女別・年齢階級別透析導入率の経年変化（2006 ～ 2021 年）
黒色の線は，報告書が発出された 2018 年以降の透析導入率の平均を示す。

③透析導入率が現状（2021 年）のままなら，将来推計人口から計算される透析導入患者数は約 4 万人となり，2028 年までに 3 万 5 千人以下という KPI は達成されない。しかし，④仮に，現状（2021 年）の全国透析導入率よりも 5％低い熊本県レベルまで透析導入率を下げることができれば，将来推計人口から計算される透析導入患者数は 3.3 万人台となり，KPI は達成される。以上より，KPI 達成のためには，これからの 5 年間で透析導入率を今以上に下げる必要があり，おおよその目安として，現状（2021 年）よりも 5％下げることが求められる。

本研究は，報告書発出前後の透析導入率の経年変化を明らかにした。2006 年～ 2021 年までの男女別年齢階級別透析導入率は，厚生労働行政推進調査事業費補助金　腎疾患政策研究事業のホームページ（https://ckd-research.jp/）で，全国および各都道府県別に公表されているが，年齢階級は 5 区分（20 歳未満，20～39 歳，40～59 歳，60～74 歳，75 歳以上）である。本研究は，細かい年齢での検討を行うことで，男女とも透析導入率のグラフは年々，右（高齢）の方へシフトしており，透析導入を先送りできていると考えられること，さらに 80 歳以上の男性では透析導入率が以前よりも上昇していることが明らかになった。すなわち，高齢男性透析患者の増加は，人口高齢化の影響だけではなく透析導入率の上昇による影響でもある。なぜ男性でのみ 80 歳以上での透析導入率が以前よりも上昇しているのかを本

Table 1　報告書発出後の 4 年間（2018 〜 2021）での予測透析導入患者数，実透析導入患者数および，その差

	男性			女性		
年齢（歳）	予測透析導入患者数	実透析導入患者数	差	予測透析導入患者数	実透析導入患者数	差
＜5	28	28	0	22	31	−9
5〜9	16	15	1	10	7	3
10〜14	14	21	−7	20	12	8
15〜19	48	49	−1	33	26	7
20〜24	183	126	57	67	65	2
25〜29	320	269	51	149	143	6
30〜34	648	636	12	297	251	46
35〜39	1,282	1,207	75	504	511	−7
40〜44	2,667	2,405	262	881	901	−20
45〜49	4,968	4,638	330	1,751	1,526	225
50〜54	6,748	6,102	646	2,232	2,122	110
55〜59	7,298	7,043	255	2,631	2,439	192
60〜64	8,973	8,694	279	3,588	3,001	587
65〜69	13,595	12,899	696	5,436	4,882	554
70〜74	18,388	17,928	460	7,313	7,082	231
75〜79	16,819	17,019	−200	7,966	7,736	230
80〜84	14,937	15,340	−403	8,414	7,994	420
85〜89	8,634	9,244	−610	5,594	5,963	−369
90〜94	2,245	2,513	−268	1,831	1,845	−14
≧95	150	256	−106	248	244	4
合計	107,959	106,437[a]	1,522	48,987	46,784[b]	2,203

[a] 年齢不明の 5 人を含む。[b] 年齢不明の 3 人を含む。

研究から明らかにすることはできないが，高齢男性は同年代の女性よりも非導入割合が低い[17]ことから，臨床現場で保存的腎臓療法ではなく透析導入を選択するような“比較的元気な”高齢者が増えているのかもしれない。2021 年のデータで，男性導入患者の約 4 人に 1 人，女性導入患者の約 3 人に 1 人が 80 歳以上での透析導入と，現状でも透析導入患者の高齢化が進んでいるが，この割合は人口高齢化により 2030 年にはさらに高まることが予測される（男性は約 3 人に 1 人，女性は約 2 人に 1 人が 80 歳以上での透析導入と推計）。本研究で認められた高齢男性での透析導入率の上昇が今後も続けば，この割合はさらに高まり，透析導入患者数増加への寄与は今以上に高まると考えられる。人生 100 年時代に，腎機能も 100 年維持できるような戦略が必要と考える。

報告書発出後の 4 年間で，透析導入率の低下により 3,725 人の透析導入を防ぐことができたと推計された。この防ぐことができたと推計された人数は年々，増加してきており，報告書発出の影響と考えるのが合理的である。透析導入患者の年間医療費を 500 万円と仮定すれば，3,725 人の減少は単純計算で医療費 186.25 億円の削減に相当する。透析に導入されなかった場合の医療費がゼロではなく，腎疾患対策に要した費用もあることから，費用対効果を単純には計算できないが，腎疾患対策は大きな削減効果を生み出すと考えられた。透析導入率の低下に，どのような要因が寄与したかを本研究からは明らかにできないが，報告書にある対策の 5 本柱，すなわち，①普及啓発，②地域における医療提供体制の整備，③診療水準の向上，④人材育成，⑤研究開発の推進が，複合的に寄与した可能性が考えられる。

一方，残念ながら現状のままでは，将来推計人口から計

Table 2　各年の予測透析導入患者数と実透析導入患者数との差

	男性				女性			
年齢（歳）	2018	2019	2020	2021	2018	2019	2020	2021
＜5	0	0	−2	2	0	−2	0	−6
5〜9	−3	2	1	1	−1	0	1	1
10〜14	−2	−5	−1	−1	3	2	3	0
15〜19	0	−2	0	1	0	−1	3	4
20〜24	11	7	19	20	−5	7	1	0
25〜29	7	18	10	15	6	−2	3	−2
30〜34	−26	19	12	7	20	3	21	3
35〜39	27	4	21	22	−15	6	10	−8
40〜44	36	42	65	119	−20	−6	−5	12
45〜49	42	23	160	105	35	28	86	77
50〜54	100	122	195	229	−35	62	35	48
55〜59	−37	105	14	174	22	31	50	88
60〜64	87	30	74	87	121	107	192	166
65〜69	8	215	191	281	108	145	150	151
70〜74	116	−31	55	319	11	−6	32	194
75〜79	−51	−65	−72	−12	39	−20	99	111
80〜84	−26	−102	−252	−24	77	130	172	42
85〜89	−22	−147	−187	−253	−45	−69	−131	−124
90〜94	−50	−52	−107	−59	26	−20	15	−35
≧95	−22	−16	−37	−32	10	−4	2	−3
合計	197	169	159	997	358	391	739	715

算される透析導入患者数は約 4 万人となり，KPI は達成されない。KPI 達成のためには，対策の 5 本柱をさらに発展させ，透析導入率のさらなる低下が必要である。熊本県の透析導入率を用いた推計結果から，これからの 5 年間で，おおよその目安として，現状（2021 年）よりも 5% 下げることができれば，KPI 達成が期待できる。性年齢を調整した透析導入率は都道府県により異なり，特定健診実施率が高い都道府県ほど低く[13]，特定健診受診者（40〜74 歳）の尿蛋白陽性割合（検尿で 1＋以上）や過体重／肥満割合〔Body body mass index（BMI）が 25 kg/m^2 以上〕とも関連する[18]。尿蛋白陽性は，5 つの健康習慣（禁煙，適正体重，節酒，活発な身体活動，健康的な食習慣）の遵守数と関連する[19, 20]ことから，都道府県により異なる尿蛋白陽性割合の一部は，不健康な健康習慣が関与している可能性がある。さらに，この特定健診で計算可能な 5 つの健康習慣の遵守数は，高血圧症や糖尿病の発症とも関連する[21]。以上より，特定健診実施率を高め，健診受診者の尿蛋白や過体重／肥満への介入，あるいは特定健診で計算可能な 5 つの健康習慣の遵守数を増やす活動などを行うことは，尿蛋白・高血圧症・糖尿病の発症予防や過体重／肥満割合の低下に繋がり，ひいては都道府県により異なる透析導入率の差を小さくし，全国の透析導入率のさらなる低下に繋がる可能性がある。

本研究の強みは，公表されているデータを用いており，新たな収集を必要としない。そのため，誰でも本研究の追試が可能である。本研究結果を解釈するにあたり，注意すべき研究の限界を以下に述べる。第一に，KPI では年間新規透析導入患者数だが，本研究の透析導入患者数には新規透析導入患者のほかに移植後再導入の患者数も含まれている。移植後再導入の患者数は 186 人と全透析導入患者の 0.5%（2021 年データ）[14]と少ないため，本研究では再導入の患者も含んだ数字を用いた。第二に，本研究では日本透析医学会統計調査の患者調査票を用いた。同統計調査では，患者調査票と施設調査票があり，両調査で導入患者数

Table 3　性・年齢階級別 2025 年および 2030 年の将来推計人口から推計した予測透析導入患者数と 2021 年透析導入患者数との差

年齢（歳）	男性					女性				
	2021 年	2025 年		2030 年		2021 年	2025 年		2030 年	
	透析導入患者数	予測数	差	予測数	差	透析導入患者数	予測数	差	予測数	差
＜20	23	22	−1	20	−3	21	20	−1	18	−3
20〜24	25	24	−1	23	−2	17	16	−1	16	−1
25〜29	65	66	1	63	−2	39	40	1	38	−1
30〜34	150	148	−2	150	0	69	67	−2	68	−1
35〜39	290	266	−24	256	−34	131	119	−12	113	−18
40〜44	512	468	−44	422	−90	197	181	−16	161	−36
45〜49	1,130	980	−150	864	−266	358	311	−47	275	−83
50〜54	1,557	1,651	94	1,413	−144	542	572	30	489	−53
55〜59	1,657	1,829	172	2,058	401	572	628	56	701	129
60〜64	2,128	2,242	114	2,443	315	718	753	35	815	97
65〜69	2,857	2,617	−240	2,748	−109	1,099	1,002	−97	1,044	−55
70〜74	4,667	3,775	−892	3,325	−1,342	1,783	1,432	−351	1,249	−534
75〜79	4,056	5,184	1,128	4,438	382	1,806	2,231	425	1,890	84
80〜84	3,897	4,259	362	5,285	1,388	2,112	2,291	179	2,720	608
≧85	3,307	3,752	445	4,409	1,102	2,176	2,376	200	2,698	522
合計	26,325[a]	27,282	957	27,918	1,593	11,643[b]	12,037	394	12,295	652

[a] 年齢不明の 4 人を含む。[b] 年齢不明の 3 人を含む。

が若干異なる（2021 年末調査[14]では，透析導入患者数は患者調査票で37,968 人，施設調査票で40,511 人と報告されている）。そのため，患者調査票を用いた本研究での推計は，低めに見積っている可能性がある。

結　語

報告書発出後も透析導入率は低下しており，対策の効果と考えられた。一方，現状（2021 年時点）での透析導入率のままでは，KPI の一つである年間新規透析導入患者数を 3 万 5 千人以下に減少は達成されない。これからの 5 年間で，現状（2021 年）よりも 5%透析導入率を下げることができれば，KPI 達成が期待できる。

利益相反自己申告：申告すべきものなし

謝　辞

本研究内容は日本透析医学会が提供する Web-based Analysis of Dialysis Data Archives（WADDA）システムを用いて著者が出力した帳票に基づいているが，結果の利用，解析，結果および解釈は発表者・著者が独自に行ったものであり，同会の考えを反映するものではない。

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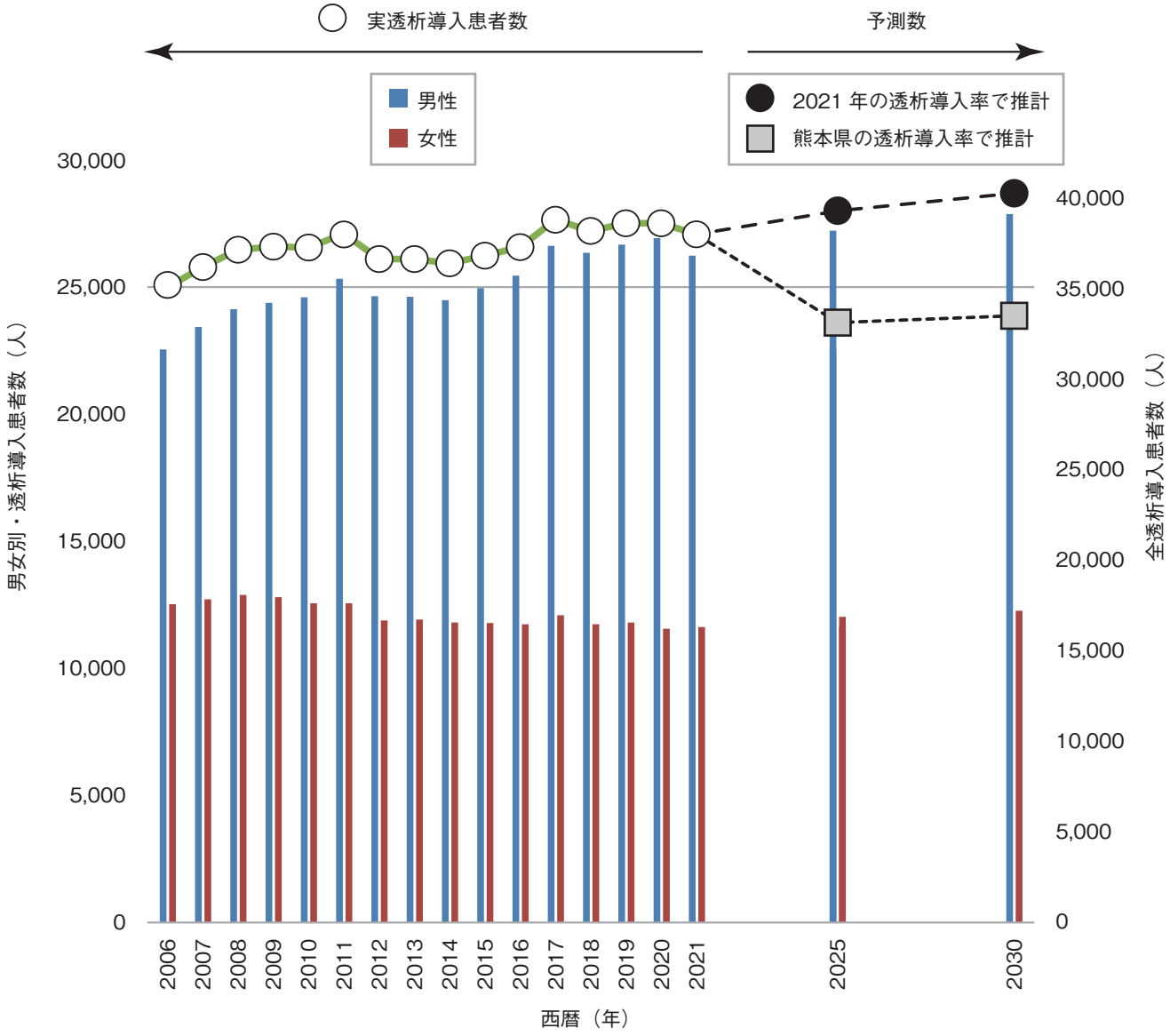

Fig. 3　2006 ～ 2021 年までの実透析導入患者数と 2025 年および 2030 年の予測透析導入患者数

2025 年と 2030 年の棒グラフは，現状（2021 年）の透析導入率のまま不変であったと仮定した場合に，将来推計人口から予測した男女別透析導入患者数を示し，●は，男女を合計した予測数を示す。
□は，現状（2021 年）の全国透析導入率よりも 5% 低い熊本県の透析導入率と将来推計人口から計算した予測数を示す。

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