学 会 等 発 表 実 績

様式第19

委託業務題目「慢性腎不全診療最適化による新規透析導入減少実現のための診療システム構築に関する研究」

機関名　筑波大学　山縣 邦弘

1．学会等における口頭・ポスター発表

発表した成果（発表題目、口頭・ポスター発表の別）	発表者氏名	発表した場所（学会等名）	発表した時期	国内・外の別
ESRD：わが国の現状と課題・口演	横山仁，杉山斉，佐藤博，山縣邦弘	東京（日本透析医学会）	2015.06.予定	国内
CKDG4～5の現状把握と重症化予防に関する最近の動向・口演	旭浩一	仙台（第8回宮城艮陵CKD研究会）	2014.11.	国内
Pathological role of palatine tonsil in IgA nephropathy	Suzuki Y, Suzuki H, Muto M, Okazaki O, Nakata J, Tomino Y	The 14th Asian Pacific Congress of Nephrology 2014	2014/5/14	国内
The pathogenetic role of tonsillar B cell producing APRIL in IgA nephropathy	Muto M, Suzuki Y, Suzuki H, Joh K, Izui S, Huard B, Tomino Y	The 14th Asian Pacific Congress of Nephrology 2014	2014/5/14	国内
Serum galactose-deficient IgA1 detected by specific monoclonal antibody KM55 is increased in IgA nephropathy patients.	Suzuki Y, Yasutake J, Suzuki H, Tomino Y	47th Annual Meeting American Society of Nephrology、Philadelphia, USA	2014/11/15	国外
IgA腎症の病因における口蓋扁桃のAPRIL産生B細胞の役割.	武藤正浩、鈴木祐介、鈴木仁、出井章三、Bertrand Huard, 富野康日己	第111回　日本内科学会総会, 東京	2014. 4.11	国内
IgA腎症惹起性IgAおよび免疫複合体産生における口蓋扁桃の役割とその制御	鈴木祐介	ワークショップ　第57回日本腎臓学会学術総会　横浜	2014. 7.4	国内
腎機能が正常にもかかわらず、血清クレアチニンの著名な高値を認めた1例	眞野訓、大澤勲、鈴木仁、井尾浩章、鈴木祐介、富野康日己.	第44回日本腎臓学会東部学術大会、東京	2014. 10. 24	国内
IgA腎症～新規バイオマーカーを用いた診断・治療選択の可能性～	鈴木祐介	よくわかるシリーズ第44回日本腎臓学会東部学術大会、東京	2014/10/24	国内
かかりつけ医師の運動習慣はCKD患者への運動指導に影響する、口頭	森下義幸，三木敦史，岡田麻里，安藤康宏，武藤重明，長田太助，草野英二	第57回日本腎臓学会学術総会	2014.07	国内
腎臓と高血圧	長田太助	第44回日本腎臓学会東部学術集会	2014.10.	国内
透析患者の血中Klotho低値は生命予後悪化の危険因子である	大谷尚子，増田貴博，秋元　哲，本間寿美子，渡邉裕子，椎崎和弘，黒尾　誠，草野英二，浅野　泰，長田太助	第57回日本腎臓学会学術総会	2014.07.	国内
CKDと呼ばれる高血圧	長谷部直幸	第57回日本腎臓学会学術総会	2014.07.	国内

腎症に対する薬物療法、口頭	四方賢一	日本都市センターホテル(日本糖尿病合併症学会第29回学術集会)	2014.10.	国内
糖尿病性腎症の診断と治療　～新たな展開～、口頭	四方賢一	アクロス福岡(第3回くすりと糖尿病学会学術集会)	2014.12.	国内
糖尿病性腎症と炎症～新規治療薬開発への道～、口頭	四方賢一	パシフィコ横浜(第57回日本腎臓学会学術総会)	2014.07	国内
GLP-1受容体作動薬の腎保護作用とその分子機構、口頭	小寺　亮	兵庫医科大学 平成記念会館(第1回日本慢性疾患重症化予防学会)	2015.02.	国内
Establishment and impacts of Japan Diabetic Nephropathy Cohort Study (JDNCS). ポスター	Furuichi K, Shimizu M, Toyama T, Wada T and The Research Group of Diabetic Nephropathy, Ministry of Health, Labour, and Welfare of Japan	伊ベルガモ(ISN NEXUS SYMPOSIUM 2014)	2014.04.	国外
Impact of anemia and renal lesions on the long-term outcomes of type 2 diabetic patients with biopsy-proven diabetic nephropathy、ポスター	Kamikawa Y, Shimizu M, Toyama T, Furuichi K, Wada T	東京(The 14th Asian Pacific Congress of Nephrology, 2014)	2014.05.	国内
Impact of Blood Pressure and Renal Lesions on the Long-Term Outcomes of Type 2 Diabetic Patients with Biopsy-Proven Diabetic Nephropathy、ポスター	Funamoto T, Shimizu M, Furuichi K, Wada T	米国フィラデルフィア(ASN Kidney Week 2014)	2014.11.	国外
高齢者腎生検施行症例の臨床的特徴　当院における100症例の検討(ポスター)	1. 伊藤 悠人, 菊田 知宏, 天野 博明, 岡山 美香, 内田 幸助, 井上 勉, 鈴木 洋通, 岡田 浩	第57回日本腎臓学会学術総会	2014.07.	国内
Geographic Difference in the Prevalence of Proteinuria and Albuminuria in Japan: Okinawa versus Ibaraki.	Nagai K, Yamagata K, Saito C, Iseki K, Asahi K, Kimura K, Moriyama T, Narita I, Fujimoto S, Tsuruya K, Konta T, Kondo M, Watanabe T.	ASN Kidney Week 2014, Philadelphia	2014.11.	国外
Annual Decline in Estimated Glomerular Filtration Rate Is a Risk of Cardiovascular Events Independent of Proteinuria.	Nagai K, Yamagata K, Saito C, Asahi K, Iseki K, Kimura K, Moriyama T, Narita I, Fujimoto S, Tsuruya K, Konta T, Kondo M, Watanabe T.	ASN Kidney Week 2014, Philadelphia	2014.11	国外
高齢者CKDの管理と治療.(口頭, 教育講演)	鶴屋 和彦	第56回日本老年医学会学術集会	2014.06.	国内
透析患者の脳血管障害Up-to-date 透析患者の認知機能障害と脳萎縮,(口頭, シンポジウム)	鶴屋和彦, 吉田寿子, 北園孝成	第59回日本透析医学会学術集会・総会	2014.06.	国内
透析患者の血圧管理を考える 体液量管理の実際～適切なドライウェイトの設定・管理の重要性～,(口頭, ワークショップ)	鶴屋和彦, 吉田寿子, 北園孝成	第59回日本透析医学会学術集会・総会	2014.06.	国内

すべてのCKD患者に向けた腎性貧血治療ガイドラインの改訂：血液透析.（口頭，コンセンサスカンファレンス）	鶴屋 和彦，山本裕康	第59回日本透析医学会学術集会・総会	2014.06.	国内
腎疾患における臓器連関の機序と病態発症における意義～脳：CKD患者の脳萎縮・認知機能低下と脳内酸化ストレス～，（口頭，シンポジウム）	鶴屋和彦，吉田寿子，藤﨑毅一郎，北園孝成	第57回日本腎臓学会学術総会	2014.07.	国内
酸塩基平衡，（口頭，よくわかるシリーズ）	鶴屋 和彦	第57回日本腎臓学会学術総会	2014.07.	国内
Increased aortic stiffness evaluated by MRI-based pulse wave velocity in patients with peritoneal dialysis: a cross-sectional and longitudinal study.(Poster presentation)	Tsuruya K, Yoshida H, Kitazono T	47th Annual Meeting of the American Society of Nephrology, Philadelphia, PA, USA	2014.11.	国外
Association of fronto-temporal gray matter volume with executive function in patients with non-dialysis dependent chronic kidney disease.(Poster presentation)	Tsuruya K, Yoshida H, Kitazono T	47th Annual Meeting of the American Society of Nephrology, Philadelphia, PA, USA	2014/11/15	国外
メタボリックシンドロームと腎. よくわかるシリーズ16（口演）	要　伸也	日本腎臓学会東部学術集会、東京	2014.10.25.	国内
糖尿病腎症4期　透析維持期までの栄養管理 透析患者における糖質栄養管理（口演）	菅野義彦	日本病態栄養学会、京都	2014/1/12	国内
免疫抑制腎移植病理と最新　Banff分類：口頭	西慎一	第47回日本臨床腎移植学会	2014	国内
Relationship between Left Ventricular Hypertrophy and Coronary Artery Calcification at the Beginning of Hemodialysis Therapy. 口頭	Kitamura K, Fujii H, Nakai K, Goto S, Nishi S	The 14th Asian Pacific Congress of Nephrology	2014	国内
Pre-transplant desensitization and the outcome of kidney transplantation of IgA nephropathy. ポスター	Yoshikawa M, Kitamura K, Kentaro N, Fujii H, Ishimura T, Fujisawa M, Nishi S	The 51th ERA-EDTA Congress	2014	国外
Relationship between glomerular filtration rate and insurin resistance in healthy subjects.ポスター	Yasumoto M Tsuda A, Ishimura E, Ohno Y, Ichii M, Nakatani S, Mori K, Fukumoto S, Uchida J, Enomoto M, Nakatani T, Inaba M	51st European Dialysis and Transplant Association Congress	2014	国外
Late-onset neutropenia and acute rejection in ABO-incompatible kidney transplant recipients receiving rituximab.	Iwai T, Uchida J, Kabei K, Kohyama Y, Okamura M, Nin Y, Iguchi K, Shimizu Y, Yukimatsu N, Yamasaki T, Kuwabara N, Naganuma T, Kumada N, Nakatani T	World Transplant Congress 2014	2014	国外

Uncontrolled home blood pressure in the morning is associated with increased urinary albumin excretion.	Kabei K, Kohyama Y, Kuwabara N, Yamasaki T, Machida Y, Naganuma T, Kumada N, Nakatani T	World Transplant Congress 2014	2014	国外
Low-Potassium Lettuce Grown with Novel Technology Can Be Safely Enjoyed Fresh by Patients on Dialysis. ポスター	Yatabe J, Yatabe MS, Takano K, Asahi K, Terawaki H, Nomaki K, Nakazawa K, Matsunaga S, Nakayama M, Watanabe	Kidney Week 2014, American Society of Nephrology	2014.11.	国外
急性腎障害の温故知新. 口頭	柴垣有吾	日本内科学会生涯教育講演会	2014	国内
超高齢社会における臨床研究で切実なアウトカムは何か？. 口頭	柴垣有吾	第57回日本腎臓学会総会	2014	国内
透析患者における酸塩基平衡異常のマネジメント. 口頭	柴垣有吾	第59回日本透析医学会学術集会・総会(シンポジウム)	2014	国内
卒後教育プログラム教育講演:拒絶反応の診断と治療. 口頭	齋藤和英	第102回日本泌尿器科学会総会	2014	国内
The role of rituximab in ABO-incompatible kidney transplantation in JAPAN. ポスター	Saito K, Takahashi K.	Kidney Week 2014, American Society of Nephrology	2014.11.	国外
Present Status of ABO incompatible kidney transplantation in Japan:口頭	Saito K, Takahashi K.	World Transplant Congress 2014	2014	国外
腎移植後CMV感染に対する顆粒球吸着療法の臨床応用. 口頭	長沼俊秀	第50回日本移植学会総会(シンポジウム)	2014	国内
腎移植後のCKD-MBDの共通性と特殊性. 口頭	長沼俊秀	第59回日本透析医学会学術集会・総会(シンポジウム)	2014	国内
当院における腎臓内科医の腎移植医療への取り組み　口頭発表　シンポジウム	谷澤雅彦、上原圭太、小板橋賢一郎、松井勝臣、山内淳司、河原崎宏雄、今井直彦、柴垣有吾、北島和樹、中澤龍斗、佐々木秀郎、力石辰也、櫻井裕子	第48回　日本臨床腎移植学会	2015	国内
Early mortality was high and was highly associated with functional status in the incident Japanese hemodialysis patients, especially in the elderly 口頭	M Yazawa, R Kido, K Kimura, S Ohira, T Hasegawa, N Hanafusa, K Iseki, Y Tsubakihara, Y Shibagaki	第51th ERA-EDTA	2014	国外
腎移植ドナーの長期管理　口頭、ワークショップ	谷澤雅彦、河原崎宏雄、今井直彦、柴垣有吾、佐々木秀郎、力石辰也、木戸亮	第47回　日本臨床腎移植学会	2014	国内
慢性腎臓病症例における血圧日内変動と腎予後の関連. 口頭	中井健太郎, 藤井秀毅, 北村謙, 河野圭志, 西慎一	第37回日本高血圧学会	2014	国内

2. 学会誌・雑誌等における論文掲載

掲載した論文(発表題目)	発表者氏名	発表した場所(学会誌・雑誌等名)	発表した時期	国内・外の別
Serum levels of galactose deficient IgA1 and related immune complex are associated with disease activity of IgA nephropathy.	Suzuki Y, Matsuzaki K, Suzuki H, Okazaki K, Yanagawa H, Ieiri N, Sato M, Sato T, Taguma Y, Matsuoka J, Horikoshi S, Novak J, Hotta O, Tomino Y.	Clin Exp Nephrol.	2014; 18:770-7	国外
Changes in nephritogenic serum galactose-deficient IgA1 in IgA nephropathy following tonsillectomy and steroid therapy.	Suzuki Y, Nakata J, Suzuki H, Sato D, Kano T, Yanagawa H, Matsuzaki K, Horikoshi S, Novak J, Tomino Y.	PLOS ONE	9(2):e89707. doi: 10.1371/journal.pone.0089707. eCollection 2014.	国外
Proposal of remission criteria for IgA nephropathy.	Suzuki Y, Matsuzaki K, Suzuki H, Sakamoto N, Joh K, Kawamura T, Tomino Y, Matsuo S	Clin Exp Nephrol.	2014; 18(3):481-486	国外
Overestimation of the risk of progression to end-stage renal disease in the poor prognosis' group according to the 2002 Japanese histological classification for immunoglobulin A nephropathy.	Miyazaki Y, Kawamura T, Joh K, Okonogi H, Koike K, Utsunomiya Y, Ogura M, Matsushima M, Yoshimura M, Horikoshi S, Suzuki Y, Furusu A, Yasuda T, Shirai S, Shibata T, Endoh M, Hattori M, Akioka Y, Katafuti R, Hashiguchi A, Kimura K, Matsuo S, Tomino Y.	Clin Exp Nephrol.	2014; 18:475-80	国外
Dietary zinc is a key environmental modifier in the progression of IgA nephropathy.	Maiguma M, Suzuki Y, Suzuki H, Okazaki K, Aizawa M, Muto M, Tomino Y.	PLOS ONE	9(2):e90558. doi: 10.1371/journal.pone.0090558. eCollection 2014.	国外
Uncoupling of glomerular IgA deposition and disease progression in alymphoplasia mice with IgA nephropathy.	Aizawa M, Suzuki Y, Suzuki H, Pang H, Kihara M, Nakata J, Yamaji K, Horikoshi S, Tomino Y.	PLOS ONE	9(4):e95365. doi: 10.1371/journal.pone.0095365. eCollection 2014.	国外
A panel of serum biomarkers differentiates IgA nephropathy from other renal diseases.	Yanagawa H, Suzuki H, Suzuki Y, Kiryluk K, Gharavi AG, Matsuoka K, Makita Y, Julian BA, Novak J, Tomino Y.	PLOS ONE	9(5):e98081. doi: 10.1371/journal.pone.0098081. eCollection 2014.	国外

Diagnosis and activity assessment of IgA nephropathy: current perspectives on non-invasive testing with aberrantly glycosylated IgA-related biomarkers.	Suzuki Y, Suzuki H, Makita Y, Takahata A, Takahashi K, Muto M, Sasaki Y, Kelimu A, Matsuzaki K, Yanagawa H, Okazaki K, Tomino Y.	Int J Nephrol and Renovasc Dis.	2014; 30(7):409-414.	国外
The kinetics of glomerular deposition of nephritogenic IgA.	Yamaji K, Suzuki Y, Suzuki H, Satake K, Horikoshi S, Novak J, Tomino Y.	PLOS ONE	9(11):e113005. doi: 10.1371/journal.pone.0113005. eCollection 2014.	国外
Enhanced auto-antibody production and Mott cell formation in Fc μ R-deficient autoimmune mice.	Honjo K, Kubagawa Y, Suzuki Y, Takagi M, Ohno H, Bucy RP, Izui S, Kubagawa H.	Int Immunol.	2014; 26:659-672.	国外
The Special IgA Nephropathy Study Group. A multicenter randomized controlled trial of tonsillectomy combined with steroid pulse therapy in patients with IgA nephropathy.	Kawamura T, Suzuki Y, Tomino Y et al.	Nephrol Dial Transplant.	2014; 29(8):1	国外
Serum under-O-glycosylated IgA1 level is not correlated with glomerular IgA deposition based upon heterogeneity in the composition of immune complexes in IgA nephropathy.	Satake K, Shimizu Y, Sasaki Y, Yanagawa H, Suzuki H, Suzuki Y, Horikoshi S, Honda S, Shibuya K, Shibuya A, Tomino Y	BMC Nephrol.	2014;15:89.	国外
Paradigm shift in activity assessment of IgA nephropathy-optimizing the next generation of diagnostic and therapeutic maneuvers via glycan-targeting.	Suzuki Y, Suzuki H, Yasutake J, Tomino Y.	Expert Opinion on Biological Therapy	2015 in press	国外
Circulating TNF Receptors 1 and 2 Are Associated with the Severity of Renal Interstitial Fibrosis in IgA Nephropathy.	Sonoda Y, Gohda1 T, Suzuki Y, Omote K, Ishizaka M, Matsuoka J, Tomino Y.	PLOS ONE	2015 in press	国外
特集　腎臓学この一年の進歩:腎炎・ネフローゼ症候群」	鈴木祐介、富野康日己	日本腎臓学会誌	2014; 56:14-21, 2014	国内
病因に基づくバイオマーカーを用いたIgA腎症の早期発見・診断・治療の試み	鈴木祐介、鈴木仁、富野康日己	Annual Review 腎臓2015	2015 in press	国内
Change of chylous ascites during low-density lipoprotein apheresis in a patient with idiopathic nephrotic syndrome	Iwazu Y, Komori S, Nagata D	Ther Apher Dial	2015;19:97-8	国外
Validation of the Japanese histologic classification 2013 of immunoglobulin A nephropathy for prediction of long-term prognosis in a Japanese single-center cohort	Sato R, Joh K, Komatsuda A, Ohtani H, Okuyama S, Togashi M, Omokawa A, Nara M, Nagata D, Kusano E, Sawada KI, Wakui H	Clin Exp Nephrol	2014.07.	国外
Primary care physicians' own exercise habits influence exercise counseling for patients with chronic kidney disease	Morishita Y, Numata A, Miki A, Okada M, Ishibashi K, Takemoto F, Ando Y, Muto S, Nagata D, Kusano E.	BMC Nephrol	2014;15:48	国外
Exercise counseling of primary care physicians in metabolic syndrome and cardiovascular diseases is associated with their specialty and exercise habits	Morishita Y, Miki A, Okada M, Tsuboi S, Ishibashi K, Ando Y, Nagata D, Kusano E.	Int J Gen Med	2014;7:277-83	国外

Positive association of vigorous and moderate physical activity volumes with skeletal muscle mass but not bone density or metabolism markers in hemodialysis patients	Morishita Y, Kubo K, Miki A, Ishibashi K, Kusano E, Nagata D	Int Urol Nephrol	2014;46:633-9	国外
Skeletal Muscle Loss Is Negatively Associated With Single-Pool Kt/V and Dialysis Duration in Hemodialysis Patients	Morishita Y, Kubo K, Haga Y, Miki A, Ishibashi K, Kusano E, Nagata D.	Ther Apher Dial	2014;18(6):612-7	国外
Prevalence of colorectal carcinoma in CKD patients in pre-dialysis and during the dialysis introduction period.	Ito C, Akimoto T, Miki T, Kusano E, Nagata D.	Clin Exp Nephrol	2015;19:148-9	国外
Microscopic polyangiitis with unilateral adrenal hemorrhage	Ito C, Akimoto T, Kusano E, Nagata D.	Intern Med	2014.09.	国外
Therapeutic Potency of Febuxostat for Hyperuricemia in Patients with Chronic Kidney Disease	Ishikawa M, Nagata D, Nakano N, Kawabata N, Akimoto T, Ishimitsu T	J Pharmacol Clin Toxicol	2014;2(3):1034-8	国外
Spontaneous spinal epidural hematoma as a potentially important stroke mimic.	Akimoto T, Yamada T, Shinoda S, Asano Y, Nagata D	J Cent Nerv Syst Dis	2014;6:15-20	国外
Hypoalbuminemia and technetium-99m-labeled human serum albumin scintigraphy	Akimoto T, Saito O, Kusano E, Nagata D	Intern Med	2014;53:1723	国外
Do we have to perform a renal biopsy? Clinical dilemmas in a case with nephrotic syndrome.	Akimoto T, Otani N, Takeshima E, Saito O, Kusano E, Nagata D	Clin Med Insights Case Rep	2014;7:67-70	国外
Impact of Metabolic Disturbances and Malnutrition-Inflammation on 6-Year Mortality in Japanese Patients Undergoing Hemodialysis.	Nakagawa N, Matsuki M, Yao N, Hirayama T, Ishida H, Kikuchi K, Hasebe N.	Ther Apher Dial	2015;19(1):30-9	国外
Cerebral Microbleeds and Asymptomatic Cerebral Infarctions in Patients with Atrial Fibrillation	Saito T, Kawamura Y, Tanabe Y, Asanome A, Takahashi K, Sawada J, Katayama T, Sato N, Aizawa H, Hasebe N.	Stroke	2014;23(6):1616-22	国外
Febuxostat for Hyperuricemia in Patients with chronic kidney disease.	Tetsu Akimoto, Yoshiyuki Morishita, Chiharu Ito, Osamu Iimura, Sadao Tsunematsu, Yuko Watanabe, Riji Kusano, Daisuke Nagata	Drug Target Omsoghts	2014; 8:39-43	国外
Clinical Implication of the Renin-angiotensin-aldosterone Blockers in Chronic Kidney Disease Undergoing Hemodialysis	Yoshiyuki Morishita, Eiji Kusono, Daisuke Nagata	The Open Cardiovascular Medicine Jouranal	2014; 8:6-11	国外
Factors associated with remission and/or regression of microalbuminuria in type 2 diabetes mellitus.	Ono T, Shikata K, Obika M, Miyatake N, Kodera R, Hirota D, Wada J, Kataoka H, Ogawa D, Makino H.	Acta Med Okayama	2014; 68(4):235-41.	国外
Lifestyle modification is associated with improving estimated glomerular filtration rate (eGFR) and proteinuria in Japanese with proteinuria	Miyatake N, Shikata K, Makino H, Numata T	Acta Med Okayama	2014; 68(1):43-6	国外
Dipeptidyl peptidase-4 inhibitor ameliorates early renal injury through its anti-inflammatory action in a rat model of type 1 diabetes.	Kodera R, Shikata K, Takatsuka T, Oda K, Miyamoto S, Kajitani N, Hirota D, Ono T, Usui HK, Makino H.	Biochem Biophys Res Commun	2014; 443(3):828-33	国外

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Ⅳ．研究成果の刊行物・別刷

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ORIGINAL ARTICLE

Proposal of remission criteria for IgA nephropathy

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Abstract
Background The remission criteria of immunoglobulin A (IgA) nephropathy have varied depending on the clinical study. Therefore, nephrologists cannot make a uniform assessment of treatment outcomes and the standardization of explanations of the condition is difficult in patients with IgA nephropathy. This study aims to propose clinical remission criteria for IgA nephropathy based on a nationwide opinion survey in Japan regarding IgA nephropathy remission/relapse.

Method This nationwide survey was sent to 312 teaching facilities of the Japanese Society of Nephrology by Progressive Renal Disease Research, Research on Intractable Disease, from the Ministry of Health, Labour and Welfare of Japan.

Results Valid answers were obtained from 193 facilities (61.9 %) (136 internal medicine facilities and 57 pediatric facilities), of which 134 (69.4 %) thought that both hematuria and proteinuria should be used in the remission standards. Approximately half of the survey respondents shared the opinion on standards of negative results for hematuria and proteinuria and the duration and frequency of these conditions.

Conclusion In this paper, we propose a standardized set of criteria for defining IgA nephropathy remission: three consecutive negative results over a 6-month period in urinary occult blood tests; urinary sediment red blood cell count of <5/high-power field (hematuria remission); and urinary protein of <0.3 g/day (g/g Cr; proteinuria remission). Clinical remission is defined as cases with both hematuria and proteinuria remission. These consensus-based remission criteria should be verified in future studies. In the meantime, they may be useful in predicting therapeutic outcome in cases of IgA nephropathy.

Keywords Remission criteria · IgA nephropathy · Hematuria · Proteinuria

For the Special IgA Nephropathy Study Group in Progressive Renal Diseases Research, Research on Intractable Disease, from the Ministry of Health, Labour and Welfare of Japan.

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Introduction

Immunoglobulin A (IgA) nephropathy is the most common form of chronic glomerulonephritis in Japan, and approximately 40 % of patients progress to renal failure within 20 years without therapeutic intervention [1]. In the past,

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one of the most popular treatments was the administration of antiplatelet agents or renin–angiotensin system (RAS) inhibitors. However, since steroid pulse therapy (TSP) was shown to be effective by Pozzi et al. [2] in 1999 and tonsillectomy combined with TSP was shown to be effective by Hotta et al. [3] in 2001, these have evolved as the standard treatments for adult, but not pediatric, patients in Japan [4]. In addition, in Japan, where annual tests for urine analysis are well developed, there are many cases in which an early diagnosis and early treatment, followed by subsequent clinical remission, are possible. However, the pathogenesis of this disease remains unclear, and thus there are many patients who show frequent relapses, or are treatment-resistant, with decreasing renal function. IgA nephropathy therefore remains a disease with a poor prognosis.

There have been several studies [5–7] reporting on the remission of IgA nephropathy; however, the degree, time period, and frequency of abnormal urinary findings vary depending on each nephrologist's definition of remission, rendering the state of the disease ambiguous. The fact that the standards for remission are ambiguous makes a uniform assessment of the treatment outcome and the standardization of the explanation of the condition difficult in patients with IgA nephropathy. A set of standard criteria for remission will therefore be useful to both patients and physicians.

The extreme endpoint for patients with kidney disease is end-stage kidney disease (ESKD), and to truly evaluate the therapeutic outcome a reduction in renal mortality rates should be the primary endpoint. However, IgA nephropathy is often diagnosed in its early stages, especially in Japan, and the progression of this disease is often slow. Therefore, observation of the endpoint (ESKD) within the period of observation in the same hospital can actually be very difficult. These facts indicate that it is necessary to define remission as a practical and clinically useful alternative outcome and use it as an effective assessment standard.

Accordingly, based on a consensus obtained through a survey of domestic nephrologists called "Opinion Survey Regarding IgA Nephropathy Remission/Relapse" by the Special Study Group (IgA Nephropathy) on Progressive Renal Diseases Research, Research on Intractable Disease, from the Ministry of Health, Labour and Welfare of Japan and related references, we propose the following IgA nephropathy remission criteria.

Subjects and methods

The survey was sent to 312 facilities (226 internal medicine facilities and 86 pediatric facilities) which are teaching hospitals in the Japanese Society of Nephrology and which also answered the "Nationwide survey on current treatments for IgA nephropathy in Japan" conducted in 2008 by the Special Study Group on IgA Nephropathy [4]. The content of the survey was determined after validation of the question and answer methods by a pilot study in members of this special study group.

Results

Valid answers were obtained from 193 facilities (61.9 %) (136 internal medicine facilities and 57 pediatric facilities). 95 facilities (50.2 %) had remission criteria of their own definition. Both hematuria and proteinuria were considered in the criteria in 81 of these facilities (87.0 %). Of the facilities without remission criteria, 53 facilities (53.5 %) were of the opinion that both hematuria and proteinuria should be emphasized, whereas 33 facilities (37.4 %) and 8 facilities (9.1 %) thought that only proteinuria or hematuria, respectively, should be emphasized.

Approximately half of the survey respondents shared the opinion that 3 consecutive negative results over a 6-month period of urine occult blood, or a urinary sediment red blood cell count of less than 5/high-power fields (HPF) for hematuria and protein ranging from (−) to (±) or less than 0.2 g/day or g/g Cr for proteinuria, should be the criteria for the remission.

Discussion and proposal

Items of remission criteria

The degree of proteinuria is important as a prognostic factor not only in IgA nephropathy but also in all renal diseases [8, 9], and there have been a substantial number of clinical research studies on renal disease [10, 11] in which both a decrease in kidney function and proteinuria have been considered as an endpoint.

However, in Japan, when IgA nephropathy is diagnosed, "chance hematuria" is observed during physical checkup in more than 70 % of cases [12]. In other words, the main initial symptom is hematuria. In Japan, where tests for urine analysis have been well developed and renal biopsies are more actively utilized than in Western countries, there are many opportunities to manage the disease from a very early stage. In addition, although both hematuria and proteinuria do not generally occur simultaneously from the early stages, both often occur together as the disease progresses and after the hematuria period has passed.

On the other hand, there are also cases in which both hematuria and proteinuria occur at the beginning of the

disease, and as time passes hematuria disappears and only proteinuria is observed. The possibility cannot be excluded that proteinuria in these patients is not an inflammatory reaction triggered by the deposition of IgA in the glomeruli, which is a defining feature of true IgA nephropathy, but depends on the so-called "common pathway" accompanying glomerulosclerosis and nephron reduction.

In the opinion survey we conducted, in the 87.0 % of facilities that had their own remission criterion, "disappearance of urinary findings" was the standard used, and 53.5 % of facilities without their own remission criteria suggested both hematuria and proteinuria as "items that should be focused on during remission." In the prognostic scores in Japan [13], both urinary abnormalities were considered as prognostic factors for IgA nephropathy. In addition, there were several studies [14, 15] demonstrating that 7–20 % of IgA nephropathy patients with hematuria alone or associated with mild proteinuria at renal biopsy showed a decrease in renal function over long-term observation. Accordingly, the persistence of hematuria is important, and remission of IgA nephropathy assessed by proteinuria alone is considered to lack validity in the light of the disease state. Based on the above observations, we have included both hematuria and proteinuria as assessment items in the present criteria.

Hematuria cutoff criteria

In the opinion survey, nearly all facilities responded that a change to negativity in a urine dipstick and less than 5 red blood cells of urinary sediment per HPF was used as a remission criteria of hematuria.

The Japanese Committee for Clinical Laboratory Standard studies is unifying the test strips' (1+) in over-the-counter urine occult blood reaction test strips as hemoglobin density of 0.06 mg/dL and red blood cells of 20/μL in the flow cytometry (FCM) technique. Since 2006, the detection sensitivity of the test paper has been mostly standardized among Japanese manufacturers [16]. If a red blood cell count of 20/μL in the FCM technique is converted to the microscopy cutoff value, it is generally 5/HPF or more (magnified 400×, 1 field of vision) [17]. From the above standards, the disappearance of hematuria is set and standardized at a urine occult blood reaction ranging from (−) to (±) and/or urinary sediment red blood cells of less than 5/HPF.

Urinary sediment microscopic examination method

The cutoff value of urinary sediment microscopy is defined as red blood cells of 4/HPF, according to the above observations; however, the lower limit of sediment red blood count (such as 1–4/HPF or less and 1–5/HPF or less) is believed to be different. Therefore, in facilities where the lower limit is 1–5/HPF or less, it is necessary to consider and assess the dipstick method for urinary blood and the FCM technique results.

False positive/negative urine occult blood reaction

When the urine occult blood reaction is measured using test paper, false positives with regard to hemoglobinuria/myoglobinuria and false negatives with regard to reducing substances, such as ascorbic acid, may occasionally occur [18]. For this reason, in the event of substantial differences in sediment red blood cell counts in the occult blood reaction in the test paper method and urinary sediment microscopy method, sediment red blood cell count takes precedence.

Proteinuria cutoff criteria

In the opinion survey, among those facilities that used a proteinuria criteria, 0.2 g/day (g/g Cr) or less was the most common cutoff in 142 facilities (73.6 %), whereas 32 facilities (16.6 %) used 0.3 g/day (g/g Cr) or less. In a past report regarding proteinuria remission, Reich et al. [5] reported that when proteinuria was controlled at less than 0.3 g/day in IgA nephropathy patients, the 15-year renal survival rate was 96 %. Hwang et al. [6] also showed that the long-term renal survival was favorable in a group in which the proteinuria level was maintained at less than 0.3 g/day through treatments.

In nephrotic syndrome, proteinuria of less than 0.3 g/day is defined as "complete remission" by the treatment policies proposed by the Special Study Group (Nephrotic Syndrome) on Progressive Renal Diseases Research, Research on Intractable Disease, from the Ministry of Health, Labour and Welfare of Japan [19]. However, in clinical trials conducted in other countries, the complete remission criteria differ, with proteinuria levels of 0.2 g/day or less as well as less than 0.3 g/day (albumin 200 mg/day) being used. Furthermore, in the Clinical Practice Guidebook for Diagnosis and Treatment of Chronic Kidney Disease 2012 by the Japanese Society of Nephrology [18], proteinuria is defined as urinary protein excretion of more than 0.15 g/day.

Considering the above observations, a consensus "proteinuria negativity criteria" in Japan has not been established. We thus compared the parameters of proteinuria with those of other diseases and defined the proteinuria cutoff value as less than 0.3 g/day. However, in the future, it will be necessary to verify the cutoff value using large-scale cohort research studies.

Duration and frequency in remission assessment

In these criteria, we considered the frequency of hospital visits by patients with IgA nephropathy for everyday medical care and the remission survey results (approximately half of the facilities provided 3 consecutive results over a 6-month period), and determined that at least 3 consecutive results over a six-month period were necessary for assessment.

There is room for debate regarding the continuity of the findings, and it can be hypothesized that there are cases in which urinalysis was conducted, but not consequently assessed as remission (did not achieve the 3 consecutive results standard). However, considering the IgA nephropathy disease state, continued negative findings for urine abnormalities are considered important during remission, and thus we defined remission as "cases in which the criteria are fulfilled 3 consecutive times".

Proposal of IgA nephropathy remission criteria

Based on the above discussion, we propose the following criteria (Table 1). In the case where the criteria are met for 3 consecutive times or more over at least 6 months, patients are classified as being in "hematuria remission" or "proteinuria remission," and both hematuria and proteinuria remission is defined as "clinical remission." Hematuria or proteinuria remission alone is designated as "partial remission." In addition, the first date on which the remission criteria are met is considered as the remission date. Specific examples of cases in which remission can (a) or cannot (b) be assessed are demonstrated in Fig. 1.

Limitations of the opinion survey

Our survey has several limitations. First, targeted facilities primarily included mid- to large-scale hospitals, with a special emphasis on facilities that could conduct early, specific treatments within the facility, such as renal biopsy and TSP. Hence, it is possible that deviations may occur in items included in the remission criteria (hematuria and proteinuria) and assessment periods and frequencies (3 consecutive times over a 6-month period). Second, because we conducted one survey per facility, in the event of differences in opinion between nephrologists within a facility, it is possible that only the opinion of the answering individual was reflected. Third, in Japan, IgA nephropathy is often diagnosed in its early stages. Therefore, present opinion may be partly based on the clinical practice of IgA nephropathy patients in early stages. In addition, the consensus-based remission criteria presented here must be verified in future studies.

Table 1 Remission criteria for IgA nephropathy

Hematuria remission
Urine occult blood reaction: (−) to (±) or
Urinary sediment red blood cells: less than 5/HPF[a]
Proteinuria remission
Proteinuria qualitative reaction: (−) to (±) or
Proteinuria amount less than 0.3 g/day (g/g Cr)
In cases where the standards are met for 2 subsequent times or more (for a total of 3 times) during at least 6 months, patients are "*hematuria remission*" or "*proteinuria remission*," and hematuria and proteinuria remission together are defined as "*clinical remission*"

[a] In the event that nonglomerular hematuria or complication with thin basement membrane disease is suspected, this possibility should be assessed

Medical care after the remission

Because the underlying mechanisms for onset and progression of IgA nephropathy are still unclear, there is currently no specific treatment for this disease. There are cases in which relapses occur in various situations, even after remission. Nephrologists should therefore carefully and periodically follow up on the urinary findings of these patients after remission under the scope of continuous medical examinations.

Practitioners providing medical care after remission need to know the criteria by which they can recognize relapse and recurrence of IgA nephropathy. "Relapse" and "recurrence" may be defined as a return of symptoms of IgA nephropathy during clinical remission and as a deterioration of symptoms without clinical remission or during partial remission, respectively. Therefore, verification and permanent establishment of the remission criteria are required; these definitions may be helpful in the process.

Proposal for long-term cohort research

This proposal is based on an opinion survey, and not on results from long-term cohort studies. Therefore, the clinical impact of the remission proposed in this report on the renal prognosis is unclear. In the future, these remission criteria should be verified using data from long-term cohort research using the ongoing Japan Kidney Disease Registry (J-KDR) and Japan IgA Nephropathy Cohort Study (J-IGACS).

For IgA nephropathy developing over the long term (e.g., 20 years), evaluation of therapeutic efficacy should be conducted according to different criteria from that for patients with shorter-term disease. Hard endpoints for the latter patients may include end-stage kidney disease or doubling of serum creatinine levels, similar to the criteria