Renal Replacement Therapy

REVIEW Open Access

A high likelihood of increase in end-stage renal disease among the Japanese HIV-infected population

Minoru Ando[1*] and Yoko Ando[2]

Abstract

Kidneys are affected by human immunodeficiency virus (HIV) infection and its associated therapies. Antiretroviral therapy (ART) has markedly reduced acquired immune deficiency syndrome–related deaths and opportunistic infectious diseases among HIV-infected patients. This contributed to their prolonged survival; however, the improvement in survival has been accompanied by an increase in the incidence of non-infectious chronic complications, including hypertension, metabolic diseases, and chronic kidney disease (CKD). Recent studies showed that estimated prevalence of any CKD and end-stage renal disease (ESRD) among HIV-infected patients is approximately 20% and 0.5%, respectively, in Japan. Both a rapid decrease in renal function and a high positive rate of albuminuria and proteinuria are clinical characteristics of HIV-infected patients. Moreover, considering higher complication rates of hypertension and diabetes compared with non-HIV-infected individuals of the similar aging, HIV-infected patients who develop CKD and ESRD are very likely to increase. Furthermore, as the survival rate is favorable after the initiation of dialysis, the cumulative number of ESRD patients is supposed to increase. The corporation for treatment of HIV-positive hemodialysis patients by general dialysis clinics will be urgently required; however, there still remain some preoccupations and prejudices about HIV *per se* in Japan, which may provoke hesitation from accepting those patients.

Keywords: Albuminuria, Cystatin C, Estimated glomerular filtration rate, Proteinuria, Urinary biomarker

Key points

- As human immunodeficiency virus (HIV)–infected patients now live longer than ever, chronic kidney disease (CKD) and end-stage renal disease (ESRD) have emerged as significant causes of morbidity and mortality among the HIV population.
- The estimated prevalence of any CKD and ESRD among HIV-infected patients in Japan is approximately 20% and 0.5%, respectively.
- As the cumulative number of ESRD among HIV-infected patients is likely to increase, a smooth corporation between HIV core hospitals and general dialysis clinics for treatment of HIV-positive dialysis patients will be necessary soon in Japan.

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Background

As of the end of 2017, the cumulative reported number of patients with HIV infection in Japan reached 30,271, and about 1400 newly infected patients are reported annually [1]. After 1996, as antiretroviral therapy (ART) was established, and as adherence to drug therapy has been improved with reductions in the frequency of administration and number of tablets to be taken, the long-time survival rate of HIV-infected patients has dramatically improved [2–4]. Therefore, HIV has become a "controllable chronic infection," but this has made early detection and treatment of non-infectious chronic complications necessary. With aging, the prevalence of hypertension, metabolic diseases, and chronic kidney disease (CKD) naturally increases in the HIV-infected population as well as in the general population, with increases in the frequency of complications related to these diseases [5–7]. Among them, CKD is a very important risk factor that affects the patient's prognosis,

because it is closely associated with the development of end-stage renal disease (ESRD), anemia, cancer, and cerebro-cardiovascular disease (CVD) [8–10].

Glomerular and tubular diseases that are often identified in HIV-infected patients are summarized in Table 1. HIV infection itself is an infectious disease that induces glomerulonephritis [11–13], and some of the key drugs of ART have renal interstitial toxicity [14, 15]. The traditional problems of HIV-associated nephropathy (HIVAN), HIV-associated immune complex kidney disease (HIVIC), and thrombotic microangiopathy (TMA) remain important because of the late diagnosis of HIV infection or the unavailability or non-response to ART even in the contemporary ART era [16]. HIV-infected individuals of African descent, especially those who have a family history of ESRD, have been recognized as having a greater risk for HIVAN, a specific histological form of focal segmental glomerulosclerosis arising from podocyte proliferation and tubular dilatation with atrophy and flattening of the tubular epithelial cells [17, 18]. Aside from direct tubular toxicity, some antiretroviral drugs for ART are associated with increased rates of dyslipidemia, hypertension, and diabetes mellitus (DM), which in turn may increase the risk of CKD [19]. Furthermore, co-infections of hepatitis C and hepatitis B potentially complicate the landscape of kidney disease in HIV [20, 21].

To sum up, aging, the presence or absence of hypertension, DM and dyslipidemia, and the history of exposure to ART are characteristically involved in the development of CKD in HIV-infected individuals [22]. With further aging of HIV-infected individuals, the prevalence of CKD in the HIV-infected population in Japan is likely to increase gradually [7, 23, 24].

This review attempted to summarize recent prevalence of CKD and ESRD, characteristics of CKD, and renal factors relevant to prognosis of the HIV-infected population, and to alert HIV experts and general physicians to a recent increasing trend for ESRD among HIV-infected patients in Japan. The content of this review article was approved by the institutional committee on research ethics (approval number: 19-SHP-rin (A)-1).

Characteristics of CKD and ESRD among HIV-infected patients in Japan

The estimated prevalence of CKD among HIV-infected patients

CKD is usually diagnosed and evaluated, based solely on the estimated glomerular filtration rate (eGFR) [25]. However, the Kidney Disease: Improving Global Outcomes (KDIGO) proposed a new classification of CKD in 2011 by taking the degree of albuminuria or proteinuria into consideration, as these have been shown to be more important than "a decrease in eGFR" in evaluating the risk of kidney disease. The severity and future risk of CKD are classified into 4 color groups (green, yellow, orange, and red) according to a table of categories consisting of 6 stages of eGFR by 3 grades of albuminuria [26]. Therefore, in June 2012, the Japanese Society of Nephrology released the CGA (C for cause, G for GFR, and A for albuminuria) classification by modifying the KDIGO guidelines for Japanese [27].

Table 1 Kidney diseases that are identified in HIV-infected patients

Diseases	Clinical characteristics
HIV-specific glomerular disease	
HIVAN	Detectable viral load, a high amount of proteinuria, albuminuria, RPGN
HIVIC	Proteinuria and/or hematuria, variable manifestation including AKI
TMA	AKI, proteinuria, hematuria with microangiopathic hemolytic anemia and thrombocytopenia
HIV-non-specific glomerular disease	
HCV-related glomerulonephritis	Proteinuria and/or hematuria, nephritic syndrome, a decrease in serum complements
Diabetic nephropathy	Proteinuria (microalbuminuria to nephrotic syndrome), a decrease in GFR
Glomerular sclerosis	Older patients, hypertension, no or low amount of proteinuria, coexistence of atherosclerotic diseases
Membranous glomerulopathy	Nephrotic syndrome; idiopathic and secondary causes associated with HBV or cancers
Minimal change disease	Nephrotic syndrome, use of NSAIDs
IgA nephropathy	Hematuria and/or proteinuria with or without renal failure
Post-infectious glomerulonephritis	Hematuria and/or proteinuria with or without renal failure
ART-associated tubular injury	
Acute tubular necrosis	Use of TDF
Cristal nephropathy	Use of IDV and ATV
Acute or chronic interstitial nephritis	Use of ATV

HIVAN HIV-associated nephropathy, *HIVIC* HIV-associated immune complex kidney disease, *TMA* thrombotic microangiopathy, *HCV* hepatitis C virus, *HBV* hepatitis B virus, *AKI* acute kidney injury, *GFR* glomerular filtration rate, *NSAID* non-steroidal anti-inflammatory drug, *ART* antiretroviral therapy, *TDF* tenofovir disoproxil fumarate, *IDV* indinavir, *ATV* atazanavir

We first reported prevalence of CKD of stages 1–5 and stages 3–5 as 14.9–87.8% and 3.5–16.2%, respectively, in Japan [23, 24, 28, 29]; however, there remained the possibility of institutional and methodological bias, as they were the results in HIV-infected patients at a single or two institutions. To determine a more actual prevalence of CKD in HIV-infected patients in Japan, a cross-sectional study was conducted in 2135 HIV-infected individuals (2008 males and 127 females, mean age 44.4 ± 11.5 years) at 5 institutions in Tokyo between April 2012 and March 2013 [30]. In this study, the prevalence of CKD stages 1–5 and stages 3–5 are 15.8% and 9.6%, respectively, according to the traditional staging system, and the prevalence of proteinuria detected by the dipstick method (≥ 1+) was 8.9%. Among the 1976 in whom urinary albumin was measured, the prevalence of albuminuria was 14.5%, and the prevalence in the green, yellow, orange, and red color groups were 79.6, 15.1, 2.9, and 2.3%, respectively, on analysis based on the CGA classification system. If the green group is assumed to be a non-CKD group, the prevalence of any CKD in HIV-infected patients is considered to be 20.4%. Similarly, 5.2% of the patients are considered to be a high-risk (orange + red) group. Prevalence of CKD among HIV-infected patients in Japan and other countries, which is documented in the literature [31–34], is summarized in Table 2.

Characteristics of CKD in HIV-infected patients in Japan

A rapid annual reduction in eGFR in HIV-infected patients

Kooij et al. showed that being HIV-infected was independently associated with greater eGFR decline (− 1.59 [95% CI, − 0.87 to − 0.24] mL/min/1.73 m^2/year in HIV-infected patients vs. − 0.69 [95% CI, − 0.91 to − 0.48] mL/min/1.73 m^2/year in HIV-uninfected individuals; P = 0.001) among 479 HIV-infected and 377 HIV-uninfected individuals (median follow-up 3.9 and 4.1 years, respectively) [35]. In Japan, Hara et al. longitudinally studied the rate of change in eGFR in 509 HIV-infected patients (598 males and 63 females, mean age 46.4 years) [36]. During the 6 years from 2008 to 2014, eGFR decreased at a mean annual rate of 2.01 mL/min/1.73 m^2. This value is about 7 times higher than 0.31 mL/min/1.73 m^2, which is the mean value of Japanese males aged 40–49 years [37].

High prevalence of proteinuria in HIV-infected patients

According to the previous report [30], the positive rate of proteinuria by the dipstick method (≥ 1+) in HIV-infected patients was 8.9% in 2135 HIV patients. On the other hand, in a survey of 332,174 people in the Japanese general population (mean age 63.6 years, 14.5% with stage ≥ 3 CKD), proteinuria was observed in 5.4% [38]. When these results are compared, the prevalence of proteinuria is higher (8.9 vs. 5.4%) in HIV-infected patients than in the general population although they were younger (mean age 44.5 vs. 63.6 years) and included a lower percentage of those with renal dysfunction (9.6 vs. 14.5% with stage ≥ 3 CKD).

The reasons for the above-described differences in kidney disease between the HIV and non-HIV groups remain unknown, but both structural and functional disorders that occur in the context of HIV infection, ART, and non-infectious chronic comorbidities might be involved [19–21, 39].

Renal factors relevant to prognosis of HIV-infected patients in Japan

Impact of the CGA classification on the prognosis

The authors analyzed the CGA classification and the cumulative incidence of a composite outcome (death due to all causes, incident CVD, or *a* ≥ 25% decline in eGFR) during a 4-year period in 661 HIV-infected individuals by the Kaplan-Meier method [40]. As a result, the incidence of a composite outcome was significantly higher in patients categorized as “orange + red” (high-risk group) than in patients categorized as “yellow + green” (low-risk group). In the Cox proportional hazards model, “being in the CGA high-risk group” alone was significantly correlated with the incidence of the composite outcome (hazard ratio [95% confidence interval]; 2.74 [1.21–5.86]). Thus, it could be recommended for HIV specialists to perform CKD risk assessment, using the CGA classification with cooperation from nephrologists.

Impact of albuminuria alone on the prognosis

The authors conducted a prospective investigation in 661 Japanese HIV-infected individuals on ART to evaluate the effects of urinary albumin excretion on the composite outcomes [41]. When albuminuria was categorized into 5 grades according to the urinary albumin-creatinine concentration ratio (ACR), ACR was 0–9 mg/g in 45.7%, 10–19 mg/gCr in 23.9%, 20–29 mg/gCreatinine (Cr) in 8.3%, 30–300 mg/gCr in 16.5%, and ≥ 300 mg/gCr in 5.6%. When each group was prospectively evaluated after 3.5 years, the grade of albuminuria was correlated with the outcomes, and an ACR of ≥ 20 mg/gCr was shown to be significantly involved. In addition, the high-normal range of albuminuria could be a predictor of near-term incidence of CKD (eGFR < 60 ml/min/1.73 m^2). Thus, reevaluation of the cutoff value of ACR could be necessary in HIV-infected individuals for assessing their clinical prognosis [42].

Impact of tubular injury on the prognosis

For early detection of kidney damage in HIV-infected individuals, it is important to pay attention to tubular injury as well as glomerular dysfunction. Drug-induced

Table 2 Prevalence of CKD among HIV-infected patients

	Cohort	Age	Year	Country	Reference
Prevalence of any CKD (stages 1–5 or risk zones ≥ yellow)					
14.9%	788 HIV	46.2 ± 11.8 (all subjects)	2010	Japan	28
15.4%	732 HIV	46.7 ± 12.0 (all subjects)	2011	Japan	23
12.9%	1482 HIV	44.2 ± 11.4 (all subjects)	2013	Japan	29
14.1%[1]	1447 HIV	44.4 ± 11.5 (all subjects)	2014	Japan	24
15.8%[1]	2135 HIV	44.5 ± 11.5 (all subjects)	2018	Japan	30
20.4%[2]	1976HIV	44.5 ± 11.5 (all subjects)	2018	Japan	30
15.5%	1239 HIV	49.2 ± 10.1 (CKD subjects) 45.1 ± 10.6 (non-CKD subjects)	2002	US	31
16.8%	322 HIV	45.2 ± 11.7 (all subjects)	2007	China	32
23.7%	224 HIV	46.4 ± 9.4 (CKD subjects) 43.6 ± 8.7 (non-CKD subjects)	2008	US	33
Prevalence of high-risk CKD (≥ stages 3 or risk zones ≥ orange)					
9.4%	788 HIV	46.2 ± 11.8 (all subjects)	2010	Japan	28
9.7%	732 HIV	46.7 ± 12.0 (all subjects)	2011	Japan	23
6.7%	1482 HIV	44.2 ± 11.4 (all subjects)	2013	Japan	29
6.6%[1]	1447 HIV	44.4 ± 11.5 (all subjects)	2014	Japan	24
9.6%[1]	2135 HIV	44.5 ± 11.5 (all subjects)	2018	Japan	30
5.3%[2]	1976 HIV	44.5 ± 11.5 (all subjects)	2018	Japan	30
3.5%	4474 HIV	43.4 (38.5–50.8) (all subjects)*	2007	Europe	34
5.6%	322 HIV	45.2 ± 11.7 (all subjects)	2007	China	32
5.9%	1239 HIV	49.2 ± 10.1 (CKD subjects) 45.1 ± 10.6 (non-CKD subjects)	2002	US	31
9.7%	224 HIV	46.4 ± 9.4 (CKD subjects) 43.6 ± 8.7 (non-CKD subjects)	2008	US	33

Prevalence without annotation is determined, according to the staging system based on the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines
[1]Prevalence is determined, according to the CGA classification, using proteinuria with estimated glomerular filtration rate
[2]Prevalence is determined, according to the CGA classification, using albuminuria with estimated glomerular filtration rate
*Age is expressed as mean ± standard deviation, except for reference 34, in which median (interquartile range) is employed

renal interstitial injury has been reported for several nucleoside reverse transcriptase inhibitors (NRTIs), a nucleotide reverse transcriptase inhibitor (e.g., tenofovir disoproxil fumarate [TDF]), protease inhibitors, and a fusion inhibitor (e.g., enfuvirtide). Among the protease inhibitors, indinavir (IDV) is notorious for its nephrotoxicity and propensity to form crystals and it has been replaced by protease inhibitors with safer drug profiles [14, 19]. Also, atazanavir (ATV) is likely associated with acute interstitial nephritis and sub-acute or chronic renal insufficiency due to granulomatous interstitial nephritis characterized by the coexistence of crystalline deposition [15]. The primary cause of TDF's renal toxicity is considered to be proximal tubular injury. TDF is actively and primarily secreted at the proximal tubule, and may induce tubular damage as a result of severe mitochondrial dysfunction [14, 19]. Although the incidence is low, acute and chronic renal failure or Fanconi syndrome may occur after the use of TDF [43, 44]. The authors measured the urinary concentrations of β_2-microglobulin (β_2M), α_1-microglobulin (α_1M), and β-D-N acetylglucosaminidase (NAG) as biomarkers that reflect tubular injury, and conducted a prospective investigation in 424 HIV-infected individuals without CKD (eGFR ≥ 60 mL/min/1.73 m^2 and negative for proteinuria) to evaluate the influences of an increases in two or more biomarker concentrations on renal function [45]. When the group with tubular injury (107 patients) was followed up prospectively for 1 year, a significant decrease in eGFR was observed compared with the group with no tubular injury. Therefore, the measurement of urinary biomarkers for identifying early kidney disease has special importance in HIV-infected patients, especially in those receiving ART including the above-described drugs [14, 15],

Impact of serum cystatin C level on the prognosis

An increase in the serum cystatin C (Cy) concentration (≥ 1.0 mg/L) is a poor prognostic factor in HIV-infected

Table 3 Renal factors relevant to prognosis of HIV-infected patients in Japan

Parameter	Risk (HR [95% CI])	Outcomes
The CGA classification	Orange + red (2.74 [1.21–5.86])	Composite outcomes
Albuminuria (ACR)	20 mg/gCreatinine ≤ (NA)	Composite outcomes
Serum cystatin C level	1.0 mg/L ≤ (6.09 [1.30–24.6])	Incidence of cancer
Urinary concentration of tubular biomarkers	Elevation of two or more biomarker concentrations (NA)	Future decrease in eGFR

Composite outcomes include all-cause mortality, incidence of cardiovascular disease, or ≥ 25% decline in eGFR
ACR urinary albumin to creatinine ratio, *Cr* creatinine, *eGFR* estimated glomerular filtration rate, *HR* hazard ratio, *CI* confidence interval, *NA* not applicable

individuals as well as in the general population [46]. Yanagisawa et al. studied 515 HIV-infected males with an HIV-RNA level below the detection limit to exclude the effect of HIV-RNA and showed that an increase in the serum Cy level (≥ 1.0 mg/L) was observed in 8.2% of the patients, which was 1/4 to 1/5 of the frequency in the USA (31–42%), and that it is significantly associated with probability of their adverse outcomes including the incidence of CVD [47]. Moreover, when this group was prospectively followed up for 3 years, an elevation of the serum Cy level was suggested to be related to the new occurrence of cancer [47, 48]. As an elevation of the serum Cy level is known to be correlated to the total mortality and the development of CVD in the general population [46], further evaluation concerning the serum Cy level in HIV-infected individuals is warranted. Table 3 summarizes clinical factors that are relevant to prognosis of HIV-infected patients.

An epidemic of ESRD among HIV-infected patients in Japan

Rasch et al. showed that the incidence of ESRD requiring any renal replacement therapy is increased more than 3- to 4-fold in the HIV-infected patients, compared with the background population in Denmark [49]. Ando et al. investigated the number of ESRD patients receiving chronic hemodialysis (HD) among the HIV-infected population across Japan, based on an HIV core hospital-based questionnaire survey [50]. There were 92 ESRD (0.45%) in the 20,448 HIV patients in 2014 (382 facilities; response rate to questionnaire, 98.2%) and 103 ESRD (0.49%) in the 21,184 HIV patients in 2015 (382 facilities; response rate, 94.8%). These patients included 10 (2014) to 15 (2015) hemophiliacs who contracted HIV infection through unheated blood products. The previous report showed that the number of ESRD patients among the HIV-infected population was 44, based on the similar HIV core hospital-based questionnaire survey in 2012 (unknown number of HIV-infected patients; 380 HIV core hospitals, and response rate to questionnaire, 50.0%) [51]. Therefore, the number of ESRD among the HIV-infected population may have increased approximately 2.3-fold over 3 years (44 to 103) in Japan (Fig. 1a). On the other hand, from another viewpoint of a dialysis facility–based questionnaire survey, the number of HIV-infected patients among the

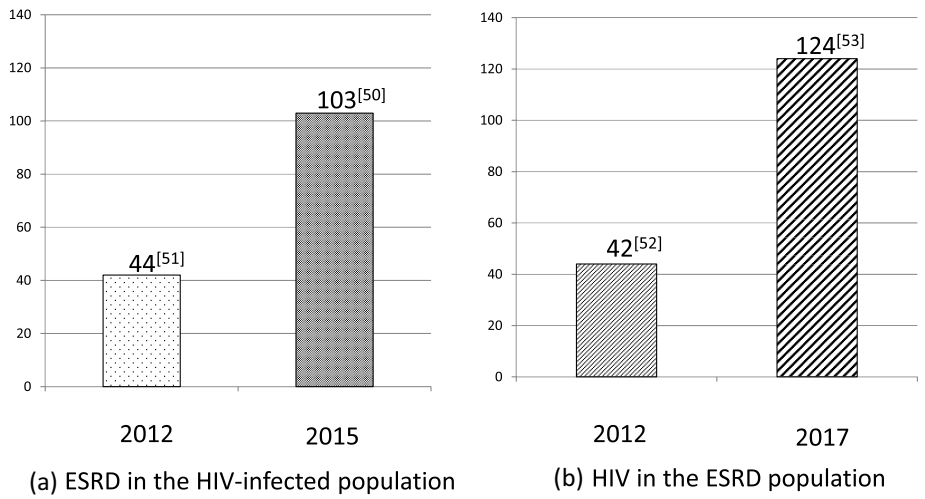

Fig. 1 An increase in the number of HIV-infected ESRD patients undergoing chronic dialysis therapy over time in Japan. **a** The number of HIV-infected ESRD patients which was examined by an HIV core hospital-based questionnaire survey: it shows a 2.3-fold increase from 2012 (43 patients) to 2015 (103 patients). **b** The number of HIV-infected ESRD patients which was examined by a dialysis facility–based questionnaire survey: it shows a 3-fold increase from 2012 (42 patients) to 2017 (124 patients). ESRD end-stage renal disease, HIV human immunodeficiency virus. Number in a bracket indicates reference number

Table 4 Prevalence of ESRD among the HIV-infected population

Prevalence	Country	Year	Cohort	References
1.03%	USA	2000	337,017 HIV	54
0.46%	Europe	2008	62,306 HIV	55
0.40%	UK	2011	28,630 HIV	56
0.19%	Germany	2010	5592 HIV	60
0.45%	Japan	2014	20,448 HIV	50
0.49%	Japan	2015	21,184 HIV	50

ESRD end-stage renal disease

ESRD population was 42 in October 2012 (in the 176,839 ESRD patients in 1951 dialysis facilities; response rate, 50.7%) [52] and 124 in October 2017 (in unknown number of ESRD patients in 1728 facilities; response rate, 44.6%) [53], respectively. This may indicate that the number of HIV-infected patients among the ESRD population increased almost 3-fold over 5 years (Fig 1b). When the prevalence of ESRD patients among the HIV-infected population in Japan in 2015 (0.49% of the 21,184 HIV-infected patients) [50] is compared with those of other advanced countries, it is less than 1.03% (of the 337,017 HIV-infected patients) in the USA in 2000 [54] but is similar to 0.46% (of the 62,306 HIV-infected patients) in Europe in 2008 [55] and 0.40% (of the 28,630 HIV-infected patients) in the UK in 2011 [56], as shown in Table 4.

Concerning the life expectancy of HIV-infected patients after the initiation of maintenance dialysis, several papers showed that 2-year survival rate is 43% in USA, 72.1% in UK, 89% in France, and 90% in Germany [57–60]. In Japan, Hara et al. executed a prognosis survey in 9 ESRD patients [61]. The median observation period after the initiation of hemodialysis was 4.6 years (range 3.5–8.9 years), and HIV infection was well-controlled during this period. When they were compared with reference patients (non-HIV-infected individuals matched for age, sex, and diabetes complication rate) who developed ESRD and began to receive hemodialysis during the same period, the 5-year cumulative survival rate after the initiation of dialysis was 88.9% and did not differ significantly compared with 79.9% in non-HIV-infected patients (P = 0.4504). Therefore, in consideration of the increase in CKD and the favorable life expectancy after the initiation of hemodialysis, the cumulative number of HIV-infected ESRD patients is very likely to increase in Japan (Fig. 2).

Some needs remain unmet in terms of acceptance of HIV-infected hemodialysis patients by general dialysis clinics in Japan. According to the latest report by the Infection Survey Subcommittee, Japanese Society for Dialysis Therapy [62], the cooperation system for treatment of HIV-infected patients at general hemodialysis clinics is inadequate. In the questionnaire survey of 4039 institutions, 215 of the 2583 institutions that responded to the survey (response rate, 64%) were requested to accept HIV-infected patients, and 87 of 215 (40%) refused the request. Also, 436 of 2583 institutions (17%) were willing to accept HIV-infected patients in the future, but 988 (38%) were not.

An increase in the number of HIV-positive ESRD patients is actual, and cooperation of general dialysis clinics in their acceptance has become necessary [52, 53, 62, 63]. It is

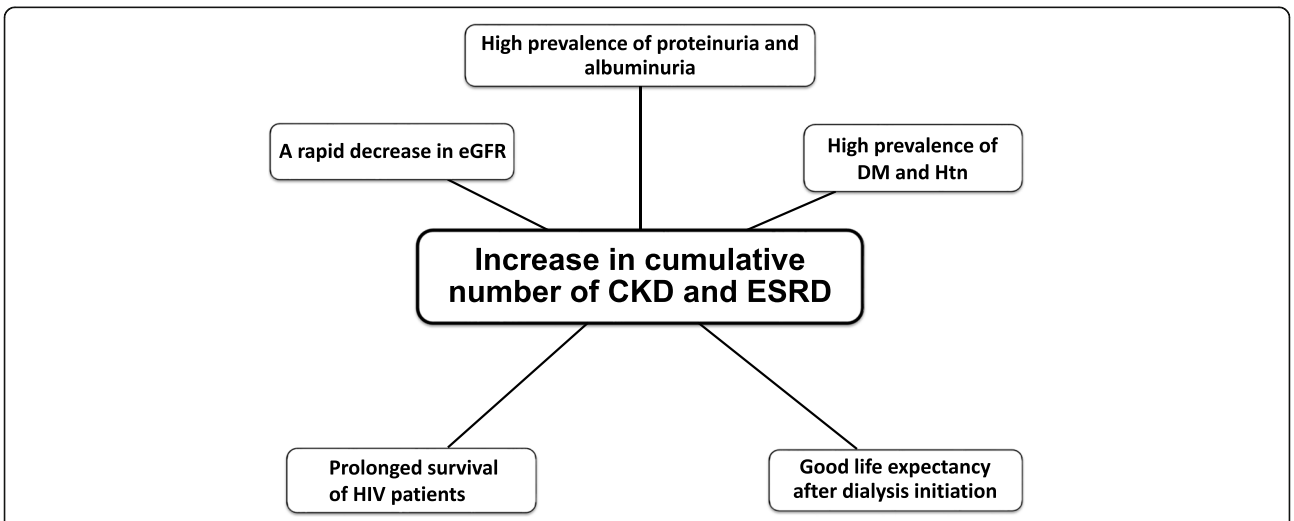

Fig. 2 The likelihood of increase in cumulative number of CKD and ESRD among the HIV population. Cumulative number of CKD and ESRD is likely increase with aging, as a rapid decrease in eGFR and high prevalence of albuminuria/proteinuria are clinical characteristics in HIV-infected patients. In addition, the prevalence of hypertension, diabetes, and dyslipidemia is higher in HIV-infected patients than in non-HIV individuals, and life expectancy after dialysis initiation is good. HIV human immunodeficiency virus, Htn hypertension, eGFR estimated glomerular filtration rate, CKD chronic kidney disease, ESRD end-stage renal disease

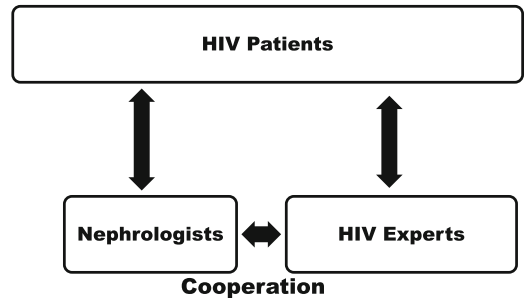

Fig. 3 How to cope with an increasing trend of CKD/ESRD among HIV patients. **H**IV experts understand that CKD is a prominent complication in the chronic period of HIV infection. They need to check urinalysis and eGFR to identify early kidney damage in their routine practice, and cooperate with nephrologists to stop growing of the number of ESRD among HIV-infected patients. CKD chronic kidney disease, ESRD end-stage renal disease, HIV human immunodeficiency virus

important first to mitigate preoccupations and prejudices about HIV itself. Then, it is urgently necessary to establish, with government support, a care system including periodic testing of HIV antibody, preparation of post-exposure prophylaxis (PEP), and reinforcement of cooperation with HIV core hospitals for the event of sudden change in the HIV-infected patient's condition.

Conclusion

HIV-infected patients who develop CKD and ESRD are expected to increase in Japan. Furthermore, as the life expectancy is favorable after the initiation of hemodialysis, the cumulative number of hemodialysis patients will also increase. It is crucial for physicians who treat HIV-infected patients to make a smooth cooperation with nephrologists to stop growing of the number of CKD and ESRD among HIV-infected patients (Fig. 3).

Abbreviations

ACR: Albumin-creatinine concentration ratio; ART: Antiretroviral therapy; CKD: Chronic kidney disease; CVD: Cerebro-cardiovascular disease; Cy: Cystatin C; eGFR: Estimated glomerular filtration rate; ESRD: End-stage renal disease; HD: Hemodialysis; HIV: Human immunodeficiency virus; NAG: N-acetyl-beta-glucosaminidase; α_1M: α_1-Microglobulin;; β_2M: β_2-Microglobulin

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