Nephrology Dialysis Transplantation

Original Article

Trends in incidence of end-stage renal disease in Japan, 1983–2000: age-adjusted and age-specific rates by gender and cause

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Abstract

Background. Trends in age-adjusted or age-specific incidence rates of end-stage renal disease (ESRD) have never been examined in Japan, a major ESRD epidemic area.

Methods. A nationwide registry has provided the number of ESRD patients commencing maintenance renal replacement therapy for time period from 1983 to 2000. We computed gender- and age-specific incidence rates of ESRD over 2-year periods, in total or by cause. Age-adjusted incidence rates were calculated using the 1985 Model Population of Japan as the standard.

Results. Causes of ESRD in 1999–2000 were, in order of decreasing frequency, diabetic nephropathy, chronic glomerulonephritis, unknown causes, nephrosclerosis and polycystic kidney disease in men, and chronic glomerulonephritis, diabetic nephropathy, unknown causes, nephrosclerosis and polycystic kidney disease in women. The age-adjusted all-cause incidence of ESRD increased until 1995–1996, but has since levelled off in both genders. The age-adjusted rate for diabetic nephropathy has been rapidly increasing, while that for chronic glomerulonephritis has decreased since 1995–1996. The former rate exceeded the latter in 1997–1998 in men. All-cause ESRD has rapidly increased in the eighties age group, whereas the increase slowed down in younger age groups in the late 1990s. The rate for diabetic nephropathy has linearly risen in almost every age group in men, whereas it began to level off in women aged 40–59 years at about 1995. For chronic glomerulonephritis, the rate had already started to decline in the mid-1980s in those aged <45 years. The rate of nephrosclerosis has been increasing independently of age.

Conclusions. The present study shows changes in the epidemiological features of the incidence of ESRD in Japan from 1983 to 2000.

Keywords: age-adjusted rate; end-stage renal disease; incidence; Japan; registry; trend

Introduction

The incidence rate of end-stage renal disease (ESRD) has been increasing both in Japan [1] and worldwide [2,3]. The annual number of patients beginning maintenance renal replacement therapy (RRT) in Japan has tripled between 1983 and 2000 [1]. In the year 2000, more than 31 000 patients began RRT in this country. To reduce the social and economical burdens involved in maintenance RRT, it is urgent to prevent ESRD. Diabetic nephropathy and nephrosclerosis have become the leading causes of ESRD in Japan [1] as in most developed countries [2–4].

To observe detailed chronological changes in the incidence of ESRD may sharpen the focus on its prevention and also suggest the aetiology of diseases leading to renal failure. The emergence of reliable RRT registries has made such studies possible, and some reports from Europe [2], North America [3] and Oceania [4,5] have already been published.

The trends in incidence, however, have been discussed mainly in terms of the annual number and relative proportion of ESRD caused by each primary disease in Japan [1,6]. Comprehensive studies including age-adjusted or age-specific rates have never been conducted in this country, one of the world's major ESRD epidemic areas [6]. The rapid increase in the older Japanese population may have partly contributed

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to the rise in incidence: the proportion of residents aged 65 years and over increased from 10.3% in 1985 to 17.3% in 2000. The age standardization of incidence rates would be useful to observe the trends independently of ageing.

We therefore determined the detailed epidemiological features of ESRD in Japan by examining the trends in age-adjusted and age-specific incidence rates by gender and cause using the data from a nationwide patient registry.

Subjects and methods

Patient registration

The registration procedures of the Patient Registration Committee of the Japanese Society for Dialysis Therapy have been described previously [1,6]. The nationwide registry covered a population of 127 million people as of 2000. The Committee mails questionnaires to all of the Japanese RRT facilities on record at the end of every year, requesting information on the case mix, laboratory data and prognostic information on each patient beginning RRT during that calendar year, as well as on all those who had been on maintenance RRT as of December 31 of the year surveyed. In each case, the attending nephrologist had determined the primary diagnosis. Registrations are believed to have been sufficiently complete. The response rate to the patient survey, defined as the proportion of RRT clinics or hospitals responding among all the facilities, was 94.6% on average (range 91.5–96.1%) between 1991 and 2000. Unfortunately, the corresponding figure was not available for every year from 1983 to 1990. It was 85.1% in 1984 and 89.5% in 1985, being somewhat lower than the rates since 1991.

In Japan, all patients on maintenance RRT are entitled to a government subsidy covering almost the entire medical cost based on the Welfare Act for the Disabled. We therefore compared the number of patients on RRT supported by the Japanese government with that registered in our database in one area that covers 5% of nationwide patients. The former ($n = 10\,929$ on April 1, 2001) was almost identical with the latter ($n = 10\,910$ on December 31, 2000), which further indicates the completeness of registration, although the nationwide number of supported patients was not available.

We may have underestimated the ESRD incidence because of incomplete nephrological referral. Thanks to the financial support, Japanese people have had the benefit of a quite open acceptance policy toward RRT since the 1970s. However, the lack of formal data in the country prevented us from quantifying the incomplete referral mainly for other than economic reasons.

Data analysis

The annual number of patients with ESRD commencing maintenance RRT stratified by gender, 5-year age group and cause of ESRD, was obtained from the registry for the 18-year period from 1983 to 2000. Populations by year, gender and 5-year age stratum in Japan were estimated based on censuses taken by the Statistics Bureau, Ministry of Public Management, Home Affairs, Posts and Telecommunications of Japan. Kidney transplantation was not considered in the present analysis because very few patients with ESRD receive a transplant in Japan [7], e.g. only 744 out of about 200 000 patients on RRT underwent renal transplantation in 2000.

In both genders, crude and age-specific incidence rates of ESRD (per million population per year) over 2-year periods (1983–1984, 1985–1986, ... and 1999–2000), in total or by cause, were computed as the number of patients starting RRT in any given 2 years divided by the corresponding population. This is because the single-year rates were unstable in some diseases and/or age categories due to the small number of cases. We did not report here the age-specific rates for polycystic kidney disease and pyelonephritis as considerable instability remained even in the rates over 2 years. The age-adjusted incidence rate by gender and cause was calculated by the direct method using the 1985 Model Population of Japan as the standard (available at http://www.ncc.go.jp/en/statistics/2001/terms/adr.html). This standard population is based on the Japanese general population in 1985 but is rounded off and smoothed for the use of age adjustment. It is defined by the Ministry of Health, Labor and Welfare of Japan and has been widely used in the country. The age-adjusted sex ratio was defined as the male-to-female ratio of the age-adjusted rate.

To save space, the age-adjusted incidence rates of ESRD by cause and the age-specific incidence rates of all-cause and cause-specific ESRD are presented by gender for the selected five 2-year periods, that is, 1983–1984, 1987–1988, 1991–1992, 1995–1996 and 1999–2000. All the relevant rates not shown in tables, however, are available from the corresponding author.

The differences between two age-specific or age-adjusted rates were statistically tested assuming a Poisson distribution of ESRD incidence [8]. We tested the rate difference between the first 2-year period (1983–1984) and the last one (1999–2000) or between 1991–1992 and 1999–2000. The latter comparison was made because we were particularly interested in the trends in the 1990s. In principle, the rate differences were tested only for these two predefined pairs of periods to avoid multiple tests. The mean age of patients commencing RRT, by gender and cause, was compared between 1983–1984 and 1999–2000 with the t test.

Results

A total of 395 059 patients who initiated maintenance RRT (239 504 men and 155 555 women) were registered during the study period from 1983 through to 2000. An additional 422 cases of unknown gender were not included in the present analysis.

The crude all-cause incidence rate of ESRD [per million population per year (PMP)] linearly increased from 116.3 to 322.9 in men and from 77.7 to 189.1 in women between 1983–1984 and 1999–2000 (Figure 1). The crude incidence rate of ESRD caused by diabetic nephropathy increased 6-fold in men and 5-fold in women from 1983–1984 to 1999–2000, while that of ESRD due to chronic glomerulonephritis has been decreasing since 1995–1996.

Among men, the commonest causes of ESRD in 1999–2000 were diabetic nephropathy [crude incidence rate, 124.4 PMP (38.5% of newly developed ESRD)], chronic glomerulonephritis [104.3 (32.3%)], unknown
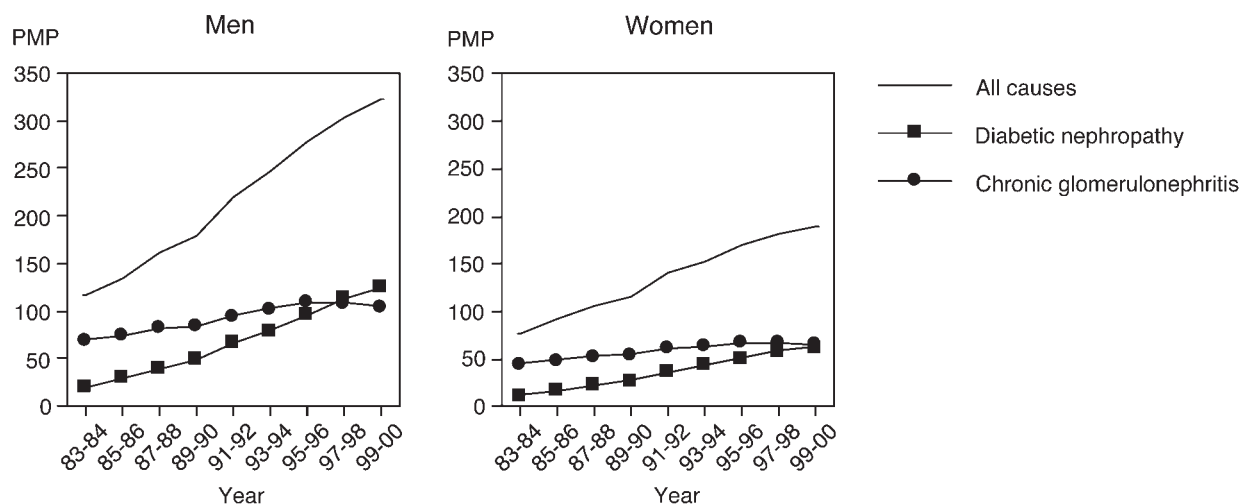
Fig. 1. Trends in crude incidence rates (PMP) of ESRD due to all causes, diabetic nephropathy and chronic glomerulonephritis by gender in Japan, 1983–2000.

or missing causes [32.4 (10.0%)], nephrosclerosis [24.1 (7.5%)] and polycystic kidney disease [6.8 (2.1%)]. Diabetic nephropathy became the leading cause in 1997–1998, replacing chronic glomerulonephritis. Among women, chronic glomerulonephritis remained the top cause even in 1999–2000 [crude incidence rate, 65.3 PMP (34.5% of new cases of ESRD)], followed by diabetic nephropathy [62.5 (33.0%)], unknown or missing causes [19.3 (10.2%)], nephrosclerosis [13.3 (7.0%)] and polycystic kidney disease [5.2 (2.7%)].

The age-adjusted all-cause incidence of ESRD had steadily increased until 1995–1996, but then began to level off in both genders (Table 1). The age-adjusted rate for ESRD from diabetic nephropathy has been the fastest growing, increasing ~4-fold in both genders between 1983–1984 and 1999–2000. On the other hand, the rate for ESRD caused by chronic glomerulonephritis has shown a downward trend since 1995–1996 in both men and women. The age-adjusted rates

significantly decreased from 1995–1996 to 1999–2000 among both men and women ($P < 0.001$). The age-adjusted incidence due to diabetic nephropathy exceeded that due to chronic glomerulonephritis in 1997–1998 in men. In women, the former rate had approached the latter by the period 1999–2000.

The crude and age-adjusted rates for ESRD of unknown or missing causes have also shown an upward trend (Figure 2 and Table 1). Although the crude and age-adjusted incidence rates for nephrosclerosis were still far below those for the top two diseases in 1999–2000, they demonstrated fast growth throughout the study period in men and women. The crude and age-adjusted rates for polycystic kidney disease have been increasing but slowly, and the age-adjusted rate has levelled off since 1991–1992. A gradually increasing crude rate and an almost fixed age-adjusted rate were observed for pyelonephritis throughout the period considered.

Table 1. Trends in age-adjusted incidence rates (per million population) of ESRD by gender and cause in Japan, 1983–2000 (rates were adjusted to the 1985 Model Population of Japan)

Gender	Year	Cause of ESRD						
		All causes	Diabetic nephropathy	Chronic glomerulonephritis	Nephrosclerosis	Polycystic kidney disease	Pyelonephritis	Unknown or missing
Men	1983–1984	123.9[a]	21.8[a]	73.6[a]	4.6[a]	3.4[a]	2.2	6.4[a]
	1987–1988	162.9	39.8	83.3	7.3	4.5	2.2	11.0
	1991–1992	205.8[a]	60.8[a]	90.1[a]	12.4[a]	5.3	2.6[b]	16.0[a]
	1995–1996	240.9	81.1	96.3	15.1	5.5	2.1	19.5
	1999–2000	254.4	96.7	84.0	18.4	5.6	2.2	25.5
Women	1983–1984	75.7[a]	11.4[a]	44.0[c]	2.0[a]	2.6[a]	1.9	4.2[a]
	1987–1988	96.4	20.8	49.0	3.2	3.3	2.2	6.2
	1991–1992	118.0[a]	29.8[a]	52.6[a]	5.4[a]	3.9	2.4[b]	9.3[a]
	1995–1996	129.0	38.2	52.7	6.5	3.9	1.9	10.0
	1999–2000	129.5	42.5	46.1	7.2	4.0	2.1	12.5

The test for rate difference compared with the rate in 1999–2000. [a]$P < 0.001$; [b]$0.01 \leq P < 0.05$; [c]$0.001 \leq P < 0.01$. The test was made only between 1983–1984 and 1999–2000 and between 1991–1992 and 1999–2000 to avoid multiple tests.
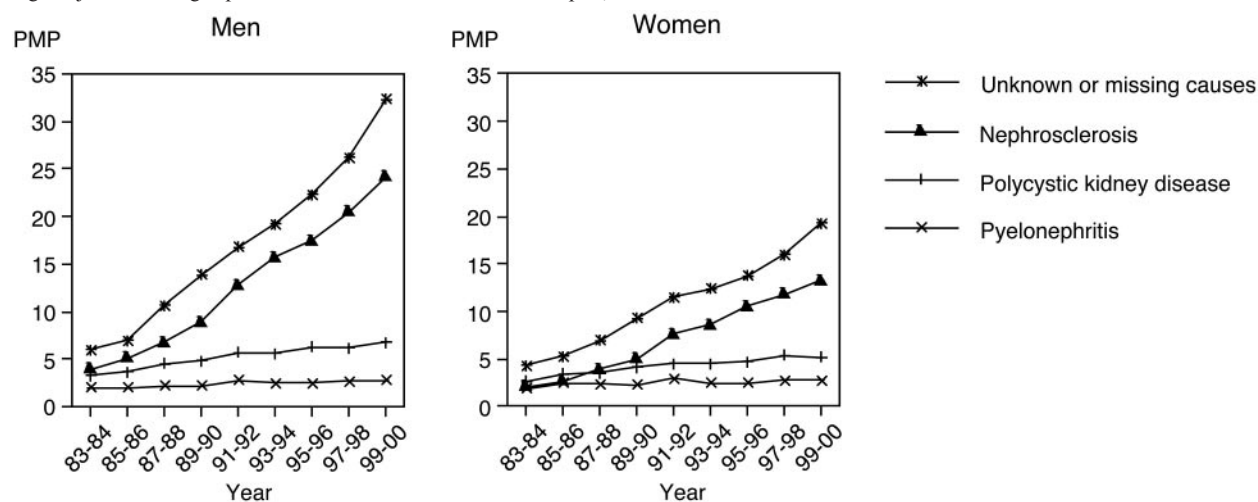
Fig. 2. Trends in crude incidence rates (PMP) of ESRD due to unknown or missing causes, nephrosclerosis, polycystic kidney disease and pyelonephritis by gender in Japan, 1983–2000. Note that the scale of the ordinate is not identical to that in Figure 1.

As for all- and major causes of ESRD, age-adjusted incidence rates for men have always been higher than those for women (Table 1). For nephrosclerosis, in particular, men were at 2.5 times as high a risk as women; the age-adjusted sex ratio was 2.39 on average from 1983–1984 to 1999–2000. The evident rise in the sex ratio for diabetic nephropathy is worthy of note: the ratio increased from 1.91 in 1983–1984 to 2.28 in 1999–2000. The sex ratio was relatively low for pyelonephritis and polycystic kidney disease, averaging 1.07 and 1.32, respectively, during the study period.

The age-specific incidence rate of all-cause ESRD has increased much more rapidly among those in their 80s than in other age groups irrespective of gender (Table 2). In contrast, the increase in rates slowed down among those in their 70s and younger groups in the late 1990s. The rate has even started to decrease, albeit gradually, but with a significant difference between 1991–1992 and 1999–2000 among women aged 25–49 years and men aged 25–29 or 35–39 years.

Trends in cause- and age-specific incidence rates of ESRD are summarized in Table 3 for diabetic nephropathy, glomerulonephritis and nephrosclerosis. The incidence rate for male diabetic nephropathy has been on a linear rise in almost every age group, whereas that for women began to level off in the 40s and 50s groups around 1995. For chronic glomerulonephritis, the rate has recently seen a decreasing trend in all age groups except for persons in their 80s, among whom the rate continues to increase. The incidence rate has started to decline earlier in younger populations; this trend dates back to the mid-1980s in men and women aged 40–44 years or less. In both genders, the rate has significantly decreased in those <55 years of age from 1991–1992 to 1999–2000.

ESRD due to nephrosclerosis has occurred mostly in the elderly, and has been very rare in people in their 40s or younger populations (<10 PMP during the study period). The rate has always been increasing independently of age, but the growth has become slower

Table 2. Trends in age-specific incidence rates (per million population) of all-cause ESRD by gender in Japan, 1983–2000

Gender	Year	Age												
		25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85–89
Men	1983–1984	62.7[a]	86.4[b]	110.4[b]	132.0[a]	168.8[a]	228.4[a]	275.5[a]	306.7[a]	347.0[a]	379.5[a]	330.0[a]	196.5[a]	143.6[a]
	1987–1988	49.7	77.1	106.3	150.7	203.8	286.3	378.3	438.0	510.1	582.1	615.8	489.5	285.1
	1991–1992	55.1[a]	73.0	111.6[b]	160.7	238.7	330.1[a]	460.8[a]	598.9[a]	685.5[a]	844.4[a]	873.8[a]	757.7[a]	537.5[a]
	1995–1996	48.9	75.7	108.9	164.8	258.3	376.5	520.7	713.1	837.5	1013.4	1170.9	1103.6	875.9
	1999–2000	41.9	72.9	97.5	155.6	247.5	373.6	512.8	722.4	957.9	1159.4	1322.8	1432.4	1204.4
Women	1983–1984	38.9[a]	54.8[a]	71.0[c]	94.1[c]	114.4[a]	136.6[a]	154.7[a]	191.2[a]	215.5[a]	216.1[a]	158.9[a]	96.9[a]	41.1[a]
	1987–1988	36.5	52.1	68.6	105.1	139.3	166.8	194.9	254.7	293.9	335.7	329.3	206.8	126.8
	1991–1992	35.5[b]	50.6[b]	76.8[b]	107.0[a]	155.4[b]	196.7	244.6[d]	314.2[a]	374.6[a]	454.9[a]	484.1[a]	389.6[a]	219.8[a]
	1995–1996	34.0	50.1	67.1	96.8	158.6	205.7	266.5	344.2	435.5	525.9	608.8	565.5	390.0
	1999–2000	28.2	41.8	63.6	86.2	136.8	198.1	260.8	354.2	439.8	566.8	673.4	711.0	503.8

The test for rate difference compared with the rate in 1999–2000: [a]$P < 0.001$; [b]$0.001 \le P < 0.01$; [c]$0.05 \le P < 0.10$; [d]$0.01 \le P < 0.05$. The test was made only between 1983–1984 and 1999–2000 and between 1991–1992 and 1999–2000 to avoid multiple tests.

Table 3. Trends in age-specific incidence rates (per million population) of ESRD due to diabetic nephropathy, glomerulonephritis and nephrosclerosis by gender in Japan, 1983–2000

Cause of ESRD	Gender	Year	Age												
			25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85–89
Diabetic nephropathy	Men	1983–1984	1.4[a]	4.6[b]	6.9[b]	14.3[b]	32.8[b]	63.6[b]	71.9[b]	76.2[b]	75.4[b]	67.1[b]	38.6[b]	18.6[b]	5.5[b]
		1987–1988	1.9	6.6	11.6	23.3	46.2	91.3	141.0	145.1	149.9	136.9	117.8	68.0	24.4
		1991–1992	2.1	6.2[b]	15.0[b]	34.4[b]	61.3[b]	122.3[b]	204.7[b]	248.1[b]	237.9[b]	240.2[b]	191.6[b]	121.9[b]	56.3[b]
		1995–1996	3.4	12.0	20.0	41.7	85.3	143.4	233.2	342.5	341.2	320.3	287.0	235.8	116.2
		1999–2000	3.2	13.0	26.4	52.7	95.4	169.4	247.2	351.3	447.6	443.6	369.3	325.8	200.2
	Women	1983–1984	2.8	5.7	5.8[b]	7.2[b]	13.4[b]	21.2[b]	28.2[b]	42.4[b]	49.7[b]	43.3[b]	26.8[b]	10.8[b]	1.4[b]
		1987–1988	3.1	5.5	8.3	14.7	23.8	39.6	50.8	71.4	95.6	94.3	67.3	24.8	13.3
		1991–1992	4.1	8.2	11.2	18.8	31.8[c]	53.0[b]	73.6[b]	104.4[b]	127.6[b]	141.2[b]	118.7[b]	56.1[b]	18.5[b]
		1995–1996	3.7	8.5	11.0	20.8	42.7	63.6	94.1	132.1	160.5	181.5	172.9	119.1	55.0
		1999–2000	3.9	6.7	13.2	19.1	37.0	69.5	92.2	149.2	185.4	216.2	213.0	188.0	91.9
Glomerulonephritis	Men	1983–1984	49.7[b]	66.2[b]	84.0[b]	93.7[b]	105.7[d]	121.4	144.5	165.4[b]	174.5[b]	192.3[b]	184.6[b]	77.2[b]	74.6[b]
		1987–1988	36.4	56.9	74.3	97.2	115.7	137.9	163.4	192.7	225.4	269.3	290.9	224.2	150.7
		1991–1992	40.3[b]	51.1[b]	70.5[b]	91.6[b]	127.3[b]	138.5[a]	164.2[c]	217.4	259.3	328.8	353.1[b]	318.6[b]	209.9[b]
		1995–1996	31.7	44.9	62.9	86.0	122.5	157.1	183.2	224.4	284.0	369.8	449.8	432.7	367.2
		1999–2000	25.4	38.2	43.3	64.2	94.2	123.9	153.8	205.5	271.0	348.6	441.2	462.9	426.2
	Women	1983–1984	25.2[b]	34.7[b]	45.4[b]	63.1[b]	73.1[b]	80.9[c]	84.7	102.6	107.1[b]	112.9[b]	80.0[b]	45.1[b]	21.2[b]
		1987–1988	21.9	30.9	40.2	61.0	79.7	87.6	94.1	116.6	127.1	148.7	159.9	104.9	65.4
		1991–1992	19.7[a]	28.1[d]	43.7[b]	57.3[b]	81.1[b]	89.2[b]	101.2[c]	122.9[d]	135.6	183.0	204.6	171.8[b]	81.4[b]
		1995–1996	17.9	27.5	35.7	48.0	75.4	88.5	102.6	118.9	154.8	190.5	229.6	236.5	160.1
		1999–2000	14.5	21.9	29.5	39.1	54.7	73.2	92.4	111.5	130.4	178.6	218.2	242.9	192.9
Nephrosclerosis	Men	1983–1984	0.1	0.3[a]	0.8[b]	0.7[b]	1.7[b]	2.9[b]	8.0[b]	13.7[b]	21.4[b]	34.9[b]	34.9[b]	39.1[b]	16.6[b]
		1987–1988	0.1	0.2	0.6	1.9	2.5	6.2	9.4	15.4	30.8	44.2	73.2	84.8	44.8
		1991–1992	0.7	1.0	1.3[a]	2.9[d]	5.0	6.8[a]	11.5[d]	24.7[a]	46.8[d]	90.5[a]	121.8[b]	153.2[b]	117.7[b]
		1995–1996	1.1	1.5	2.2	3.6	5.8	9.0	14.7	27.8	49.6	102.4	161.6	192.8	184.3
		1999–2000	0.5	1.8	3.3	5.2	5.8	10.8	15.1	32.5	55.3	112.7	196.7	278.0	249.7
	Women	1983–1984	0.0[c]	0.1	0.1[d]	0.5[d]	1.2[a]	1.5[b]	2.6[b]	4.7[b]	9.6[b]	15.2[b]	17.9[b]	13.8[b]	7.1[b]
		1987–1988	0.0	0.0	0.6	0.8	1.4	2.3	2.9	6.2	12.7	22.2	37.5	33.5	22.5
		1991–1992	0.1	0.4	0.5	1.4	1.2[a]	2.8[d]	7.9	10.3	20.1	36.4	55.6[b]	70.2[b]	52.0[b]
		1995–1996	0.4	0.6	0.5	1.4	2.5	3.5	5.9	12.6	21.8	43.5	72.4	85.5	88.4
		1999–2000	0.3	0.3	0.9	1.7	3.4	4.8	7.2	11.1	22.4	41.6	79.5	110.8	95.3

The test for rate difference compared with the rate in 1999–2000: [a]$0.001 \leq P < 0.01$; [b]$P < 0.001$; [c]$0.05 \leq P < 0.10$; [d]$0.01 \leq P < 0.05$. The test was made only between 1983–1984 and 1999–2000 and between 1991–1992 and 1999–2000 to avoid multiple tests.

since 1995, particularly in women 60–74 years of age (Table 3).

The incidence rates of ESRD have been rising in particular in the 80s group (Tables 2 and 3), which may substantially affect the trends in age-adjusted incidence rates for all ages. We therefore compared the age-adjusted rates for all ages with those for <80 years, that is, age-adjusted rates computed excluding the 80s group. The trends, however, were quite similar in the two age-adjusted rates (data not shown). Accordingly, the trends in age-adjusted sex ratios (the male-to-female ratio of the age-adjusted rate) for all ages were comparable with those for <80 years.

Between 1983–1984 and 1999–2000, the mean (median) age (in years) of male patients starting RRT increased from 52.3 (53) to 63.3 (65) for all causes, from 56.7 (56) to 62.8 (64) for diabetic nephropathy, from 50.1 (50) to 62.0 (64) for chronic glomerulonephritis, from 53.3 (54) to 65.4 (67) for unknown or missing causes, from 67.0 (69) to 71.9 (74) for nephrosclerosis, from 52.2 (53) to 59.3 (58) for polycystic kidney disease and from 54.1 (57) to 62.0 (65) for pyelonephritis. The mean (median) age of female patients also rose from 53.3 (54) to 65.1 (67), 58.0 (60) to 65.6 (67), 51.9 (52) to 63.8 (66), 55.9 (57) to 67.9 (71), 68.1 (70) to 74.6 (77), 55.4 (55) to 59.4 (59) and 53.5 (55) to 61.8 (64), correspondingly, during the same period. The increase in mean ages reached statistical significance for all causes, diabetic nephropathy, chronic glomerulonephritis and unknown or missing causes in both genders ($P < 0.001$) and for polycystic kidney disease in men ($P = 0.046$).

Discussion

We have documented here the age-adjusted and age-specific trends in ESRD incidence rates in Japan over 18 years using data from a patient registry. The strengths of the present study are thanks to the nationwide, high-quality RRT registry available in Japan. By calculating the age-adjusted or age-specific rates, we were able to take into account the ageing of our study population.

Some methodological issues need elucidation. First, some patients with ESRD might not have undergone RRT, and therefore we may have underestimated the ESRD incidence. The acceptance policy toward RRT seems to have been very open since the 1970s in Japan. Nevertheless, the incidence rate of ESRD in the 80s group showed an exceptionally faster growth than those in younger populations, which may partly be explained by policy changes regarding the elderly with renal failure. The trends in age-adjusted rates and sex ratios, however, were virtually unaltered when we restricted the analysis to those <80 years of age. This may mean that the increase in the incidence rate in the 80s group had relatively little effect on the overall trends when the ageing of the Japanese population is considered.

The improved survival rate of RRT for ESRD due to diabetic nephropathy [9] may have encouraged nephrologists to accept more patients with the disease. This would have resulted in a spurious rise in the incidence rate of ESRD, in addition to the authentic increase due to the upsurge of diabetic patients in Japan [10].

Secondly, the response rate of the patient survey by the registry was slightly lower in 1984 and 1985 compared with that between 1991 and 2000, which would have increased the incidence rates of ESRD by 5–10% between 1984–1985 and 1991–2000.

The potential misclassification of the primary causes of ESRD may be another limitation. The attending physician of each patient performed the diagnosis given in the Japanese RRT registry. Moreover, only 6% of new ESRD cases in 2000 were diagnosed based on histological findings. It would not be easy to accurately differentiate nephrosclerosis from chronic glomerulonephritis without renal biopsy findings. Thus, the possible changing pattern in diagnostic practice may have affected the trends in ESRD incidence caused by the two diseases. Most of the decline in the incidence rate of ESRD due to chronic glomerulonephritis, however, cannot be ascribed to misclassification because the incidence rate of ESRD caused by nephrosclerosis has been far lower than that caused by chronic glomerulonephritis, especially among those in their 50s or younger.

Finally, type 1 diabetes was not differentiated from type 2 disease for almost all the incident cases of ESRD, so that we could not report the incidence rates by type of diabetes.

All-cause incidence of ESRD

The crude all-cause incidence rate of ESRD has constantly been increasing in both genders, whereas the age-adjusted one started to level off in 1995–1996. This means that the rise in the crude incidence rate of ESRD in recent years is due largely to the ageing of the Japanese population.

The rapid increase in incidence rates in the elderly has been observed in Europe [2], the US [3], Australia and New Zealand [4] as well as in Japan. During the study period from 1983 to 2000, life expectancy at birth increased from 74.20 to 77.72 years among men and from 79.78 to 84.60 years among women in Japan (http://www.mhlw.go.jp/toukei/saikin/hw/life/life02/sanko-2.html). Those in their 80s now, therefore, may not be selectively healthy people but those with more complications including renal insufficiency. In the same period, life expectancy at age 80 years also rose from 6.36 to 7.96 years among men and from 7.69 to 10.60 years among women in Japan. This improvement may alter nephrologists' attitude toward RRT, so that they accept more elderly patients.

The levelling off in the age-adjusted rate at the end of the last decade in Japan and the US [3] is in contrast with the continuing linear increase in European countries other than The Netherlands [2]. The recently decreasing rates in those in their 40s or younger

groups, especially in women, have resulted in the levelling off of the overall age-adjusted rate in Japan. Observations should be continued to verify the trends because this levelling off, if true, is very important for projection of future trends and for health care planning.

Diabetic nephropathy

The incidence rates of ESRD due to diabetic nephropathy, both crude and age-adjusted, have steadily been increasing in Japan.

The elevation in the crude rate appeared to have accelerated, especially in men, starting in about 1990 (Figure 1). This may be explained by the sharp increase in prevalence of diabetes mellitus in Japan starting around 1980 [10] if we allow for a 10-year time lag between the increases in diabetes and diabetic nephropathy. The prevalence of diabetes in men aged 40 years or over was estimated to be 1.6% in 1970, 2.7% in 1980, 6.0% in 1990 and 14.0% in 2002 [10,11]. The percentages in women were 0.9% in 1970, 1.6% in 1980, 4.0% in 1990 and 7.9% in 2002.

The age-adjusted rate nearly doubled over the latest 10 years as well as in Europe [2] and the US [3]. The age-adjusted rate for diabetic nephropathy in Japan (97 PMP in men and 43 in women in 1999–2000) is lower than in the US (157 in men and 133 in women in 1998–2001) but is much higher than in Europe (27 in men and 20 in women in 1998–1999). This comparison, however, should be interpreted with caution because of the difference in the standard population for age adjustment between Japan, the US and Europe. In addition to differences in the prevalence of diabetes [12], the management of diabetic patients, and the acceptance of RRT for diabetic nephropathy, differences in genetic susceptibility to nephropathy may cause geographical variations in rates. The incidence rate of nephropathy in early-onset Japanese patients with type 2 diabetes is estimated to be similar to or even higher than that in Caucasian patients with type 1 diabetes of comparable age [13].

The greater incidence of ESRD from diabetic nephropathy among males seems peculiar to Japan: men were at twice as high a risk as women in Japan, whereas the male-to-female ratio in age-adjusted incidence rate was under 1.4 in Western countries [2,3]. We found a notable elevation in the age-standardized sex ratio (men/women) of the incidence rate in the late 1990s. The prevention of diabetic nephropathy among men, therefore, should be stressed in Japan.

Chronic glomerulonephritis

The age-adjusted incidence rate of ESRD attributable to chronic glomerulonephritis started to decline in 1995–1996 in Japan but has remained stable in Europe [2] and the US [3]. Our examination of the age-specific rate data clearly showed the earlier reduction in the risk of ESRD in younger men and women. This cannot be related to the increased rates of ESRD due to unknown or missing causes because the magnitude of the decline in rates for chronic glomerulonephritis among the under 45 years age group far exceeded the magnitude of the increase in rates for unknown/missing causes (4–27 times the increase for unknown/missing causes). The decrease in risk may be partly due to improved screening and treatment of glomerulonephritis, which may delay the development of renal failure. Another explanation may be that any possible decline in the incidence of chronic glomerulonephritis had occurred long before the decrease in ESRD incidence. Most chronic glomerulonephritis occurs in younger populations [14]. Any decline in its incidence, therefore, may have decreased the ESRD rate earlier in the young than in the middle-aged and elderly. The possible decrease in incidence of chronic glomerulonephritis, particularly of immunoglobulin A (IgA) nephropathy, might be related to widespread use in Japan of antibiotics for common colds to prevent severe infections of the upper respiratory tract, or the gradual westernization of the Japanese diet [15].

Although decreasing, the age-adjusted incidence rate of ESRD caused by chronic glomerulonephritis in Japan (84 PMP in men and 46 in women in 1999–2000) is still far higher than in Europe (23 in men and 10 in women in 1998–1999) [2] and the US (39 in men and 21 in women in 1998–2001) [3]. The higher risk in Asian people may be related to the higher rate in Japan: Asian Americans show more than twice as high a risk as Caucasians in the US [3]. The low percentage (10% of ESRD due to chronic glomerulonephritis) of histologically confirmed diagnoses in Japan would be an additional explanatory factor as the incidence was highest when this percentage was lowest in Europe [2].

Nephrosclerosis

The incidence rate of ESRD caused by nephrosclerosis has been on a rising trend among men and women 50 years or older. This upward trend in each age-specific rate indicates that the increase in new cases of ESRD due to nephrosclerosis cannot simply be explained by the ageing of the Japanese population.

The incidence rates due to hypertension and vascular disease also rose particularly in those 65 years and over in Europe [2] and Australia [5]. In the US, the age-adjusted rate for ESRD from hypertension has been extremely high (116 PMP in men and 66 in women in 1998–2001) [3] compared with those in Europe [16 (men) or 7 (women) in 1998–1999] [2] and Japan [18 (men) or 7 (women) in 1999–2000]. The different coding system makes direct comparisons difficult between registries [16]. The decreasing but still high stroke mortality rates in Japan [17] may suppress the incidence of ESRD in patients with hypertension as a competing risk.

Some patients diagnosed previously as chronic glomerulonephritis may now be classified as nephrosclerosis, a change that would apparently raise the

incidence of ESRD caused by nephrosclerosis. If the increase in incidence is not due to such a change in diagnosis, it would be inconsistent with the declining trend in blood pressure in Japan [18], presumably due to the more widespread use of anti-hypertensives. However, the drugs used extensively in Japan, such as calcium channel blockers, might not be sufficiently effective for nephrosclerosis, compared with angiotensin-converting enzyme inhibitors [19]. Another possibility may be that more patients with hypertension would now survive long enough to develop nephrosclerosis owing to the decline in other fatal complications such as stroke [17]. The increasing incidence of ESRD due to nephrosclerosis with a lowering prevalence of hypertension has also been observed in Europe [2,20] and Australia [5,21]. Further studies to address this inconsistency would be helpful for the prevention of nephrosclerosis.

Polycystic kidney disease and pyelonephritis

For polycystic kidney disease, the incidence rate of ESRD has been only very gradually increasing during the 1990s in Japanese as in Europeans [2] and Americans [3]. The age-standardized rate in Japan (5.6 PMP in men and 4.0 in women in 1999–2000) is somewhat lower than in Europe (7.8 in men and 6.0 in women in 1998–1999) and the US (8.7 in men and 6.9 in women in 1998–2001), but the gap becomes smaller when the Japanese rate is compared with that in American Asians (6.5 and 5.3, correspondingly).

The age-adjusted sex ratio was lower for ESRD due to polycystic kidney disease compared with ESRD due to other causes excluding pyelonephritis. The ratio (1.32 on average) was, however, still greater than unity, and is comparable with the ratios (1.2–1.3) in other countries [2,3,22]. Because almost all cases of polycystic kidney disease result from an autosomal genetic abnormality [22], men and women should have equal incidence rates. The slight male predominance in ESRD incidence, therefore, would reflect the poorer prognosis in men [23]. More precise determination of the factors predisposing men to ESRD will afford useful information to avert ESRD caused by polycystic kidney disease.

The age-adjusted incidence rate of ESRD attributable to pyelonephritis in Japan (2.2 PMP in men and 2.1 in women in 1999–2000) was much lower than that due to tubulointerstitial nephropathy in Europe (10.6 in men and 8.6 in women in 1998–1999) [2]. The differences in disease classification and genetic background may partly account for this gap. Widespread use of antibiotics in Japan could have prevented some ESRD caused by urological infections.

In conclusion, age-adjusted and age-specific examinations into the incidence rates could clarify the epidemiological features of ESRD in Japan and provide the basis to predict future trends.

Conflict of interest statement. None declared.

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