

## CORRESPONDENCE



## Risk of Human T-Cell Leukemia Virus Type 1 Infection in Kidney Transplantation

**TO THE EDITOR:** Human T-cell leukemia virus type 1 (HTLV-1), a retrovirus infecting 5 million to 10 million people worldwide, can cause the incurable neurologic disorder HTLV-1-associated myelopathy–tropical spastic paraparesis (HAM–TSP) as well as adult T-cell leukemia–lymphoma.<sup>1,2</sup> Although case reports document the development of these debilitating diseases after kidney transplantation, the incidence of HTLV-1 infection after kidney transplantation and related complications is unknown, and screening for HTLV-1 is not performed in most countries.<sup>3,4</sup> We conducted a nationwide survey in Japan, one of the countries in which HTLV-1 is endemic.<sup>2</sup>

Using data from the Japanese Renal Transplant Registry, which records all kidney transplantations in Japan,<sup>5</sup> we identified 180 transplantations between 2000 and 2014 in which the donor, the recipient, or both were HTLV-1–positive. In February 2016, questionnaires inquiring about the onset of HAM–TSP and adult T-cell leukemia–lymphoma were sent to the hospitals in which the transplantations were performed. The rate of response to the questionnaire was 55.0% (for 99 transplantations), and the median post-

transplantation follow-up duration was 4.5 years (range, 0.1 to 13.4) (Table 1).

HAM–TSP developed in 4 of the 10 HTLV-1–negative recipients of transplants from HTLV-1–positive donors (40%); the risk of HAM–TSP in this group was much higher than that among either HTLV-1–positive recipients who received transplants from HTLV-1–positive donors (0 of 30) or HTLV-1–positive recipients who received transplants from HTLV-1–negative donors (1 of 59 [2%]). Among HTLV-1–negative recipients of transplants from HTLV-1–positive donors, the median incubation period before the development of HAM–TSP was 3.8 years (range, 1.3 to 8.4); there were no cases of adult T-cell leukemia–lymphoma in this group. Furthermore, seroconversion after kidney transplantation was confirmed in 7 of the 8 (87%) negative recipients who received a transplant from a positive donor (data on 2 patients were not available). In contrast, neither HAM–TSP nor adult T-cell leukemia–lymphoma developed in any of the 30 positive recipients of transplants from positive donors. Among the 59 positive recipients who received transplants from negative donors, 1 had both HAM–TSP and adult T-cell leukemia–lymphoma, which developed at 8 and 10 years, respectively, after kidney transplantation. The only confirmed HTLV-1–related death was the single patient who died from adult T-cell leukemia–lymphoma.

Our survey showed a high risk of HTLV-1 transmission and HAM–TSP development after a short incubation period in HTLV-1–negative recipients of kidney transplants from HTLV-1–positive donors, in contrast with the low risk of HTLV-1–associated diseases in HTLV-1–positive recipients of kidney transplants from either

### THIS WEEK'S LETTERS

- 296 Risk of Human T-Cell Leukemia Virus Type 1 Infection in Kidney Transplantation
- 298 Coronary CT Angiography and Subsequent Risk of Myocardial Infarction
- 301 Brain Change in Addiction as Learning, Not Disease

**Table 1. Characteristics and Outcomes of the Kidney Transplant Recipients for Whom Complete Data Were Available.\***

Characteristic or Outcome	Overall (N=99)	Donor Positive, Recipient Negative (N=10)	Donor Positive, Recipient Positive (N=30)	Donor Negative, Recipient Positive (N=59)	P Value†
Median post-transplantation follow-up (range) — yr	4.5 (0.1–13.4)	6.4 (1.3–13.3)	4.1 (0.8–13.4)	4.6 (0.1–13.1)	0.93
Living-donor transplant — no. (%)	85 (86)	10 (100)	29 (97)	46 (78)	0.03‡
Median age at transplantation (range) — yr	53.0 (15–71)	44.0 (15–66)	52.0 (26–70)	54.0 (19–71)	0.17
Male sex — no. (%)	57 (58)	6 (60)	19 (63)	32 (54)	0.76
HTLV-1 seroconversion after transplantation — no.					
Present	—	7	—	—	—
Absent	—	1	—	—	—
Data not available	—	2	—	—	—
HAM-TSP — no. (%)	5 (5)	4 (40)	0	1 (2)	<0.001§
Median time from transplantation to HAM-TSP (range) — yr	5.4 (1.3–8.4)	3.8 (1.3–8.4)	—	8.3	0.48
ATLL — no. (%)	1 (1)	0	0	1 (2)	1.00
Time from transplantation to ATLL — yr	10.2	—	—	10.2	—
Death — no. (%)	15 (15)	1 (10)	4 (13)	10 (17)	0.92
Median time from transplantation to death (range) — yr	5.3 (0.1–12.9)	2.4	4.4 (0.8–11.1)	6.6 (0.1–12.9)	0.73
Kidney failure — no. (%)	18 (18)	3 (30)	5 (17)	10 (17)	0.54
Median time from transplantation to kidney failure (range) — yr	5.0 (0.0–11.7)	4.0 (1.0–9.3)	0.7 (0.0–10.0)	6.2 (0.0–11.7)	0.81

\* A total of 180 transplantations in which the donor, the recipient, or both were positive for human T-cell leukemia virus type 1 (HTLV-1) were identified: 27 involving a positive donor and a negative recipient, 46 involving a positive donor and a positive recipient, and 107 involving a negative donor and a positive recipient; only those 99 transplantations for which data from the questionnaires were available are included in the table. ATLL denotes adult T-cell leukemia-lymphoma, and HAM-TSP HTLV-1-associated myelopathy-tropical spastic paraparesis.

† Differences among the three groups were assessed with the Kruskal-Wallis test for continuous variables and Fisher's exact test for categorical variables. P values were two-sided and were considered to indicate statistical significance when less than 0.05.

‡ P values for additional comparisons, corrected for multiplicity by the Bonferroni method, were as follows: for transplantation from an HTLV-1-positive donor to an HTLV-1-negative recipient as compared with a positive donor to a positive recipient, P=1.00; from a positive donor to a negative recipient as compared with a negative donor to a positive recipient, P=0.57; and from a positive donor to a positive recipient as compared with a negative donor to a positive recipient, P=0.09.

§ P values for additional comparisons, corrected for multiplicity by the Bonferroni method, were as follows: for transplantation from an HTLV-1-positive donor to an HTLV-1-negative recipient as compared with a positive donor to a positive recipient, P=0.007; from a positive donor to a negative recipient as compared with a negative donor to a positive recipient, P=0.003; and from a positive donor to a positive recipient as compared with a negative donor to a positive recipient, P=1.00.

HTLV-1-positive or HTLV-1-negative donors. These data suggest that HTLV-1 screening of donors and recipients could be of value before kidney transplantation when donors are from HTLV-1-endemic areas. Kidney transplantation from a positive donor to a negative recipient carries a high risk of infection. Given that both the newly infected and the previously infected transplant recipients received immunosuppressive agents, the high risk of HAM-TSP only in HTLV-1-negative recipients receiving a transplant from a positive

donor may indicate that a lack of anti-HTLV-1 immunity is an important risk factor for HAM-TSP after receipt of a kidney transplant from a positive donor. Future studies with a longer follow-up period may better quantify the risk of adult T-cell leukemia-lymphoma in kidney transplant recipients.

Junji Yamauchi, M.D., Ph.D.

Yoshihisa Yamano, M.D., Ph.D.

St. Marianna University School of Medicine  
Kawasaki, Japan

Kenji Yuzawa, M.D., Ph.D.

National Hospital Organization Mito Medical Center  
Ibaraki, Japan  
kyuzawa@aol.com

Supported by a Health and Labor Sciences Research Grant on Rare and Intractable Diseases from the Ministry of Health, Labor, and Welfare of Japan (H26-nanchi-shitei-113, H27-nanchi-shitei-101, H28-nanchi-ippan-018) and a grant from the Practical Research Project for Rare and Intractable Diseases of the Japan Agency for Medical Research and Development (JP18ek0109356).

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

1. Poiesz BJ, Ruscetti FW, Gazdar AF, Bunn PA, Minna JD, Gallo RC. Detection and isolation of type C retrovirus particles

from fresh and cultured lymphocytes of a patient with cutaneous T-cell lymphoma. *Proc Natl Acad Sci U S A* 1980;77:7415-9.

2. Gessain A, Cassar O. Epidemiological aspects and world distribution of HTLV-1 infection. *Front Microbiol* 2012;3:388.

3. Gallo RC, Willems L, Hasegawa H, Global Virus Network's Task Force on HTLV-1. Screening transplant donors for HTLV-1 and -2. *Blood* 2016;128:3029-31.

4. Kaul DR, Davis JA, AST Infectious Diseases Community of Practice. Human T cell lymphotropic virus 1/2 in solid organ transplantation. *Am J Transplant* 2013;13:Suppl 4:355-60.

5. Yagisawa T, Mieno M, Yoshimura N, Yuzawa K, Takahara S. Current status of kidney transplantation in Japan in 2015: the data of the Kidney Transplant Registry Committee, Japanese Society for Clinical Renal Transplantation and the Japan Society for Transplantation. *Ren Replace Ther* 2016;2:68.

DOI: 10.1056/NEJMc1809779

## Coronary CT Angiography and Subsequent Risk of Myocardial Infarction

**TO THE EDITOR:** Newby et al. (Sept. 6 issue)<sup>1</sup> report the ability of coronary computed tomographic angiography (CTA) to reduce cardiovascular mortality. The authors (reporting for the Scottish Computed Tomography of the Heart [SCOT-HEART] investigators) hypothesized that the immediate improvement in outcomes was related to coronary revascularization,<sup>2</sup> whereas the long-term benefit was derived from statins.<sup>1,2</sup> However, differences in medical management were rather modest to account for such big differences in outcomes, as indicated in the accompanying editorial.<sup>3</sup> With revascularization procedures, on the other hand, a substantial increase of approximately 40% was observed in standard-care patients after the first year.<sup>1</sup> A central question, which is not addressed by the authors, is the time sequence of the late revascularization procedures and cardiac end points. If late revascularization procedures were performed in patients with acute conditions or after infarction in patients receiving standard care, this outcome would imply that earlier intervention in the CTA group contributed at least partially to improved outcomes. If, on the other hand, late revascularization procedures were performed in a more elective setting before the occurrence of cardiac end points, the role of early revascularization would lose importance and would justify the allocation of early prevention strategies to higher priority in future studies and in clinical practice.

Grigorios Korosoglou, M.D.

Sorin Giusca, M.D.

GRN Hospital Weinheim  
Weinheim, Germany  
gkorosoglou@hotmail.com

No potential conflict of interest relevant to this letter was reported.

1. SCOT-HEART Investigators. Coronary CT angiography and 5-year risk of myocardial infarction. *N Engl J Med* 2018;379:924-33.

2. SCOT-HEART Investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. *Lancet* 2015;385:2383-91.

3. Hoffmann U, Udelson JE. Imaging coronary anatomy and reducing myocardial infarction. *N Engl J Med* 2018;379:977-8.

DOI: 10.1056/NEJMc1816189

**TO THE EDITOR:** The SCOT-HEART investigators report that coronary CTA plus standard care versus standard care alone in patients with stable chest pain resulted in a rate of death from coronary heart disease or nonfatal myocardial infarction that was 1.6% lower at 5 years. The investigators hypothesize that event reductions were mediated by an uptake of appropriately targeted preventive therapies on the basis of coronary CTA findings. However, as shown in Figure 3 of the article, available at NEJM.org, an elevated ASSIGN score (a prespecified cardiovascular risk score that ranges from 1 to 99, with higher scores indicating a higher risk of cardiovascular dis-