Erectile function and its impact on quality of life in Japanese men on hemodialysis

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Abstract: The objective of this study was to characterize the erectile function and its impact on health-related quality of life (HRQOL) in Japanese men on hemodialysis. This study included 65 consecutive Japanese men <80 years on hemodialysis. Erectile function and HRQOL were evaluated using the Sexual Health Inventory for Men (SHIM) and the Short-Form 8 (SF-8) survey, respectively. These 65 men were classified into 54 with SHIM ≤11; relatively severe erectile dysfunction (ED) (group A) and 11 with SHIM ≥12; relatively mild ED (group B). There were significant differences in age, marital status, ankle-brachial index (ABI), and serum levels of free testosterone and prolactin between groups A and B. Of several factors examined, age, marital status and ABI were significantly associated with the severity of ED on univariate analysis, and of these 3 factors, only age was significantly associated with severity of ED on multivariate analysis. SF-8 survey revealed that all scale scores in group A were inferior to those in group B. Comparatively severe ED appeared to be frequently observed in Japanese men on hemodialysis, and this trend was marked in elderly men. Furthermore, the severity of ED had a negative impact on the wide range of HRQOL in these men.

Subjects: Aging and Health; Andrology & Men's Health; Dialysis; Impotence & Sexual Dysfunction; Quality of Life; Sexual and Reproductive Health

Keywords: erectile function; hemodialysis; quality of life; SHIM; SF-8

ABOUT THE AUTHORS
Mainly, our research activities are concentrated on male infertility and men's health, including erectile dysfunction and late-onset hypogonadism. This article is the first step of our research for understanding the status of erectile function and its impact on health-related quality of life in Japanese men on hemodialysis. The subsequent step will be the development of methods for improving erectile dysfunction in order to contribute to ameliorate health-related quality of life in these men.

PUBLIC INTEREST STATEMENT
In recent years, the prognosis of patients on chronic hemodialysis has been markedly improved, resulting in the growing significance of quality of life in these patients. The prevalence of erectile dysfunction (ED) in men on hemodialysis has been reported to be very high, and ED is regarded as one of the most important disorders that may have a negative impact on both physical and mental conditions in men. In this study, therefore, we investigated the status of erectile function and its impact on the health-related quality of life (HRQOL) in Japanese men on hemodialysis. We showed that comparatively severe ED appeared to be frequently observed in Japanese men on hemodialysis, and this trend was marked in elderly men. Furthermore, the severity of ED had a negative impact on the wide range of HRQOL in these men.
1. Introduction
In recent years, the prognosis of patients on chronic hemodialysis (HD) has markedly improved, resulting in the growing significance of quality of life (QOL) in these patients (Rosas et al., 2003). Erectile dysfunction (ED), defined as the persistent inability to attain an erection sufficient to permit satisfactory sexual performance (Hatzimouratidis et al., 2010), is regarded as one of the most important disorders that may have a negative impact on both physical and mental conditions in men. The prevalence of ED has been reported as being between 70 and 86% in men undergoing chronic HD (Arslan et al., 2002; Miyata et al., 2004; Neto, de Freitas Rodrigues, Saraiva Fittipaldi, & Moreira, 2002; Türk et al., 2004); however, in routine clinical practice, insufficient attention has been paid to problems associated with sexual functions in this cohort of patients (Al Khallaf, 2010). It has been well documented that physiological and psychological risk factors related to chronic HD, including anemia, uremic neuropathy, hypogonadism, hyperprolactinemia, hyperparathyroidism, atherosclerosis and depression, play important roles in the development of ED (Ayub & Fletcher, 2000; Chou et al., 2001; Gómez, De La Cueva, Wauters, & Lemarchand-Béraud, 1980; Lawrence et al., 1997; Palmer, 1999). In addition, some other factors, such as medication, diet, lack of sleep and inadequate dialysis, are reported to influence a patient’s erectile function (Diemont et al., 2000; Milde, Hart, & Fearing, 1996; Palmer, 1999). However, there has been limited information with respect to the impact of such risk factors on the severity of ED in men undergoing chronic HD.

In this study, therefore, we included a total of 65 consecutive Japanese men who underwent chronic HD therapy for at least 3 months, and evaluated the erectile function with the Sexual Health Inventory for Men (SHIM), one of the most widely used tools to identify and grade the severity of ED (Heruti, Ashkenazi, Shochat, Tekes-Manova, & Justo, 2005), and the association between several factors and the severity of ED in these patients. In addition, we investigated the status of health-related QOL (HRQOL) using the Medical Outcomes Study 8-Item Short-Form Health Survey (SF-8), a recently developed tool for the assessment of QOL providing a measurement of 8 health-related domains (Turner-Bowker, Bayliss, Ware, & Kosinski, 2003), in these men according to the severity of ED.

2. Methods
After excluding patients who were treated with androgen deprivation therapy or had undesirable complications, such as terminal cancer and severe acute illness, this study included a total of 65 consecutive Japanese men ≤80 years who received chronic HD for at least 3 months at our institution. The study protocol was approved by the Ethical Committee of our institution. Written informed consent to be included in this study was obtained from all patients prior to their participation.

In this series, we evaluated several demographic variables and clinical data in each patient, including age, marital status, duration of hemodialysis, body mass index (BMI), systolic and diastolic blood pressures, presence of diabetes mellitus (DM) and a history of cardiovascular disease (CVD). Blood examinations, including of hemoglobin, albumin, free testosterone, prolactin, calcium, phosphate and intact parathyroid hormone levels, were performed. In addition, ankle-brachial index (ABI) was measured to evaluate the degree of peripheral arterial disease (PAD).

In this study, ED was assessed using the SHIM, which is an abridged version of the International Index of Erectile Function (IIEF) used to evaluate the erectile function domain only, that is commonly used in urology studies (Heruti et al., 2005). ED was classified into the following categories based on the score of SHIM: without ED (22–25), mild ED (17–21), mild to moderate ED (12–16), moderate ED (8–11) and severe ED (≤7). In addition, the surveys of Hospital Anxiety and Depression Scale subscales for depression (HADS-D) (Zigmond & Snaith, 1983) and SF-8 (Fukuhara & Suzukamo, 2004) were also conducted in these men to assess their depression status and HRQOL, respectively. HADS-D is a self-assessment scale that has been developed and found to be reliable for detecting states of depression in the setting of a hospital medical outpatient clinic. As previously reported (Fukuhara & Suzukamo, 2004), SF-8 contains eight self-administered questions for the quantification of HRQOL using eight multi-item scales, namely, physical function (PF), role limitations because of physical health problems (RP), bodily pain (BP), general health perception (GH), vitality (VT), social
function (SF), role limitations because of emotional problems (RE) and mental health (MH). These eight scales were scored separately from 0 to 100, with higher scores indicating better health status. These domain scores were standardized using Japanese population norms to have a mean score of 50 and a standard deviation of 10.

All statistical analyses were performed using Statview 5.0 software (Abacus Concepts, Inc., Berkeley, CA), and \( p < 0.05 \) was considered significant. Differences were compared using unpaired t-test and chi square test. Logistic regression analysis was used to determine the association between several parameters and the severity of ED.

### 3. Results

According to the findings on SHIM, 47 men (72.3\%) had severe ED, 7 (10.8\%) moderate, 6 (9.2\%) mild/moderate and 2 (3.1\%) mild. Only 3 men (4.6\%) were without ED. In addition, 65 men were classified into 54 (83.1\%) with SHIM \( \leq 11 \); relatively severe ED (group A) and 11 (16.9\%) with SHIM \( \geq 12 \); relatively mild ED (group B). Table 1 summarizes the baseline characteristics of the 65 men included in this study according to the severity of ED. There were significant differences in several parameters, including age, marital status, ABI, and serum levels of free testosterone and prolactin, between groups A and B.

To minimize the influence of valid characteristics on the ED surveys in this cohort of men, the contribution of several factors to the severity of ED was evaluated by uni- and multivariate logistic regression analyses (Table 2). Univariate analysis showed that age, marital status and ABI were significantly associated with the severity of ED; however, only age appeared to have an independent impact on the severity of ED on multivariate analysis.

| Table 1. Clinical and biological characteristics of patients | Total (n = 65) | Relatively severe ED (n = 54) | Relatively mild ED (n = 11) | \( p \)-value |
|---|---|---|---|---|
| Age (years) | 62.8 ± 11.8 | 65.1 ± 9.8 | 51.5 ± 14.6 | <0.001 |
| Marital status with a partner, \( n \) (%) | 44 (68) | 38 (86) | 4 (36) | 0.002 |
| Duration of hemodialysis (months) | 130 ± 110 | 132 ± 112 | 122 ± 104 | 0.77 |
| Body mass index (kg/m\(^2\)) | 21.9 ± 3.2 | 22.1 ± 3.3 | 21.4 ± 3.1 | 0.18 |
| Systolic blood pressure (mmHg) | 151 ± 24 | 152 ± 24 | 148 ± 22 | 0.63 |
| Diastolic blood pressure (mmHg) | 82 ± 15 | 81 ± 14 | 84 ± 17 | 0.65 |
| Diabetes mellitus, \( n \) (%) | 17 (26) | 16 (30) | 1 (9) | 0.30 |
| Cardiovascular disease, \( n \) (%) | 13 (20) | 12 (27) | 1 (9) | 0.38 |
| Ankle-brachial index standard value (0.9–1.4), \( n \) (%) | 19 (29) | 15 (28) | 4 (36) | 0.02 |
| Depression no (HADS-D \( \leq 7 \)), \( n \) (%) | 36 (55) | 27 (50) | 9 (82) | 0.11 |
| Hemoglobin (g/dL) | 11.1 ± 0.8 | 11.2 ± 0.9 | 11.0 ± 0.6 | 0.09 |
| Albumin (g/dL) | 3.6 ± 0.4 | 3.6 ± 0.3 | 3.8 ± 0.5 | 0.18 |
| Free testosterone (pg/mL) | 4.6 ± 2.4 | 4.3 ± 2.2 | 6.4 ± 2.8 | 0.04 |
| Prolactin (ng/mL) | 35.3 ± 51.9 | 38.6 ± 56.4 | 19.8 ± 9.5 | 0.03 |

Notes: ED, erectile dysfunction; HADS-D, the surveys of Hospital Anxiety and Depression Scale subscales for depression.
The outcomes of HRQOL surveys using SF-8 are shown in Figure 1. All eight scale scores in group A were inferior to those in group B, and a significant difference between these two groups was noted only in the RE score.

4. Discussion
To date, a number of studies have reported the high prevalence of ED in men undergoing chronic HD. For example, Fernandes et al. (2010) showed that 72.3% of men who were treated with HD therapy were diagnosed with ED. In recent years, remarkable progression has been achieved in the field of HD therapy, resulting in growing interest in the issues associated with QOL rather than prognosis (Rosas et al., 2003). Furthermore, ED is regarded as one of the potential risk factors unfavorably affecting the satisfactory status of daily life in men receiving chronic HD therapy; however, limited information concerning the erectile function in Japanese men on HD, particularly the impact of ED on the QOL...
status, is available. In this study, therefore, we conducted a prospective evaluation of erectile function and its impact on HRQOL in a total of 65 consecutive Japanese men who underwent HD therapy.

In this series, 83% of the Japanese men on HD were diagnosed with moderate or severe ED based on the SHIM scores. This clearly indicates that the prevalence of ED in these men is much higher than that in the standard population of Japanese men, despite being assessed using a method to detect ED that differs from SHIM (Marumo, Nakashima, & Murai, 2001). To date, several studies have shown that various factors play important roles in the development of ED in these patients, such as uremic milieu, peripheral neuropathy, autonomic insufficiency, peripheral vascular disease, pharmacologic therapy and psychological stress (Anantharaman & Schmidt, 2007; Procci, Goldstein, Adelstein, & Massry, 1981; Toorians et al., 1997). In this study as well, significant differences in several parameters, including age, marital status, ABI, and serum levels of free testosterone and prolactin, were noted between the relatively mild and severe ED groups. Collectively, these findings suggest that more complicated factors might be involved in the pathogenesis of ED in men on HD than that in those with normal renal function.

It is of interest to identify factors potentially influencing the severity of ED in men undergoing chronic HD; accordingly, we assessed the significance of several parameters as possible factors having an impact on the severity of ED by using logistic regression analyses. Of those examined in this study, only age was shown to be independently correlated with the severity of ED irrespective of the remaining parameters. There have been several studies indicating that age was the most significant risk factor for ED in renal failure patients (Arslan et al., 2002; Nassir, 2010; Naya et al., 2002; Neto et al., 2002). For example, Arslan et al. (2002) stated that the prevalence and severity of ED by decade showed significant increases as age increased. However, despite the lack of a significant association with the severity of ED in this series, DM was also identified as an independent risk factor of ED in men receiving HD in various previous studies (Fernandes et al., 2010; Naya et al., 2002; Rosas et al., 2001). These conflicting findings concerning the impact of DM on the erectile function in men on HD might be due to the low incidence of DM in patients included in this study.

Another point of interest is the effect of erectile function on the QOL in men receiving HD therapy. In this series, the SF-8 survey of the HRQOL status in the 65 Japanese men showed that all of the 8 scale scores in the relatively mild ED group were superior to those in the relatively severe ED group, and that there was a significant difference in the RE score between these two groups. Although the HRQOL could have been affected by a wide variety of factors, such as age, disease type, therapeutic efficacy, adverse events, healthcare system and cultural background, regardless of pathological conditions, these findings suggest that the severity of ED has a negative impact on the wide range of HRQOL in men undergoing chronic HD. To our knowledge, only one study has identified an association between the severity of ED and HRQOL in men undergoing chronic HD (Fernandes et al., 2010). In this study as well, men with severe ED were shown to have a poorer HRQOL than those with mild ED.

Here, we would like to emphasize several limitations of this study. Firstly, this was a non-randomized study including a small number of patients conducted at a single institution. Secondly, although there are several well-validated multiple survey systems for the assessment of erectile function and HRQOL, only SHIM and SF-8, respectively, were used in this study. In addition, it might be preferable to use the data on HRQOL from healthy controls rather than those from age-matched controls to present more clear results about the effect of HD on HRQOL. Finally, this study included Japanese men alone, who have been reported to have features with respect to the status of erectile function that differ from those in Western populations (Collaborative Depression & Sexual dysfunction (CDS) in Hemodialysis Working Group, 2011); therefore, it might be difficult to apply the findings of this study to all cohorts undergoing chronic HD.
In conclusion, the proportion of Japanese men on HD who are diagnosed with comparatively severe ED was shown to be high, and this trend was marked in the elderly population. Furthermore, the severity of ED negatively affected the wide range of HRQOL status in Japanese men on HD.

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Competing Interests
The authors declare no competing interest.

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