Published in final edited form as:

Semin Dial. 2017 May ; 30(3): 277–281. doi:10.1111/sdi.12588.

Twice-Weekly Hemodialysis in China: Can It Be A Better Option for Initiation or Maintenance Dialysis Therapy?

Yucheng Yan^{*}, Sylvia Ramirez[†], Shuchi Anand[‡], Jiaqi Qian[§], and Li Zuo[¶]

^{*}DaVita Hospital Management Consulting (Shanghai) Co. Ltd., Shanghai, China

[†]DaVita Healthcare Partners Inc, Singapore

[‡]Division of Nephrology, Stanford University School of Medicine, Palo Alto, CA, USA

[§]Department of Nephrology, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

[¶]Peking University People's Hospital, Beijing, China

Abstract

Cumulative evidence indicates it may be worthwhile revisiting the twice-weekly hemodialysis (HD) regimen as a valid option for individualized or incremental treatments for selected patients with end-stage renal disease. In this article, we will review the current evidences on the potential pros and cons of twice-weekly HD compared to thrice-weekly HD including China's experience in the practice of twice-weekly HD. A prudent patient selection and close dialysis adequacy monitoring might be necessary for this medical treatment choice. More randomized prospective controlled studies for the critical evaluation of twice-weekly dialysis are encouraged.

Thrice-weekly hemodialysis (HD) has been considered as a “standard” HD treatment regimen among most nephrologists in the developed countries. Nevertheless, twice-weekly HD regimen continues to be prevalent in many developing countries, and even occasionally in some developed countries. In China, around a quarter of the HD population receives twice-weekly HD (1), whereas this regimen may be routine for half or even greater proportions of patients in many other South-Asia countries (2). Furthermore, thrice-weekly HD per se has been established without randomized controlled studies. Although twice-weekly HD regimen is often regarded as suboptimal, cumulative evidence indicates it may be worthwhile revisiting the twice-weekly HD regimen as a valid option for individualized or progressive treatments for selected ESRD patients. In this article, we will review the current evidence on the outcome of twice-weekly versus thrice-weekly HD including China's experience.

Address correspondence to: Yucheng Yan, MD, PhD, Baoland Plaza, B-19F, Suite 6, 588 Dalian Road, Yangpu District, Shanghai 200082, China, or yucheng.yan@163.com.

Conflict of Interest: The authors have no conflicts of interest to declare.

Effect of Twice-weekly Dialysis on Mortality

Although it is usually assumed that twice-weekly dialysis has inferior outcomes compared with thrice-weekly HD, some previous studies reported similar survival rate between the two groups of patients. A retrospective study by Hanson et al. in 1999 included 4888 incident and 10,179 prevalent HD patients from the United States Renal Data System (USRDS) and reported 24% lower mortality risk in patients on twice-weekly HD compared to those on thrice-weekly HD (3). Fernandez-Lucas et al. also reported that patients who started dialysis undergoing a twice-weekly HD regimen had a better survival rate and lower rate of residual kidney function (RKF) loss compared to those who started on a thrice-weekly regimen (4). However, when looking into the baseline data, some confounders were identified; older age, female, higher serum albumin levels, lower serum creatinine levels, lower body mass index, and shorter dialysis vintage were found more frequently in the twice-weekly group of Hanson's study and greater RKF and fewer comorbid conditions at dialysis initiation were associated with twice-weekly HD in Fernandez-Lucas's study. Although some confounders were adjusted in the analysis, the persuasiveness of the study was limited.

Our previous study with the data from Shanghai Dialysis Registry showed similar 2-year mortality between the two HD treatment frequencies (5). In addition, longer survival time in twice-weekly HD patients was observed in two subgroup analysis with 639 incident patients (692 ± 7 days vs. 667 ± 10 days, $p = 0.01$) and with 673 patients who had more than 5 years of dialysis vintage both with similar ages and RKF (704 ± 9 days vs. 689 ± 6 days, $p = 0.03$), respectively. One of the explanations may be that the patients staying on twice-weekly HD for more than 5 years may have better self-management of fluid and diet intake as well as blood pressure control compared to those on thrice-weekly dialysis.

On the other hand, several contradictory studies indicated that patients on thrice-weekly HD had a better survival than those on twice-weekly dialysis (6–8). In an observational study of 2428 patients, less frequent HD was associated with shorter patient survival; weekly treatment time of less than 8 hours was an independent risk factor (6). Interestingly, the author did not provide a relative risk analysis for the 12 hours threshold which was considered as the standard weekly duration for thrice-weekly HD. It also remained unclear whether higher mortality was associated with shorter treatment duration or less frequent HD schedules.

Another prospective study showed a marginally better survival rate in patients on thrice-weekly HD than in those on twice-weekly HD (89% vs. 85%, $p = 0.06$) (7). Hwang et al. reported an adjusted mortality of twice-weekly HD patients with RKF that was similar to those without RKF undergoing thrice-weekly HD. Twice-weekly HD patients with RKF had a far higher mortality risk than thrice-weekly patients with RKF (HR, 4.20; 95% CI: 1.0–17.3) (8). Unlike peritoneal dialysis (PD) where a gradual increment of dialysis dose is recommended to replace the loss of RKF (9), few clinical practice guidelines for HD dosage and frequency are based on RKF despite the fact that the effect of delivered dialysis dose on mortality is strongly dependent on the RKF just as it is with PD (10).

It is worthwhile to note that none of the above studies were randomized or controlled. As patient survival is influenced by multiple factors, whether or not survival is reflected by the dialysis regimen itself or patients' underlying health status remains uncertain. It is quite possible that the effect of twice-weekly HD on mortality depends on the balance of favorable or unfavorable factors which physicians consider when prescribing treatment frequency. Table 1 shows the potential favorable and unfavorable effects of twice-weekly HD regimen on patient's outcome, including mortality, hospitalization, and quality of life (QOL). An analysis using longitudinal data from the China Dialysis Outcomes and Practice Patterns Study (DOPPS) to evaluate survival and hospitalizations in patients on twice-weekly HD versus thrice-weekly HD, stratified by their RKF, is ongoing and its results may yield further insight on the outcomes for these two HD regimens.

Potential Favorable Effect of Twice-weekly Dialysis

Preservation of RKF

Contributions of RKF to mortality may be much more important than those of dialysis dosage or frequency (10). A growing body of literature has demonstrated that RKF among patients on either PD or HD not only plays an important role in solute and fluid removal, diet intake, electrolyte balance, blood pressure control, bone metabolism, and red blood cell production, but also is closely associated with better survival and higher QOL (2). However, in contrast to the great efforts to reduce RKF loss among PD patients, the role and protection of RKF has not been the subject of a similar concern in HD patients. Recently the Frequent Hemodialysis Network Nocturnal Trial, where a half of patients showed urine volume 500 ml/day at baseline, reported that RKF declined faster in the six-times weekly HD group than in the thrice-weekly HD group (11), stressing the need for considering the preservation of RKF when prescribing dialysis dose to HD patients with RKF.

A small study from Taiwan (12) reported that patients on twice-weekly HD had a slower decline of RKF versus those on thrice-weekly HD after an 18-month period of follow-up. Fewer intradialytic hypotensive episodes and hospitalizations were also found in twice-weekly HD patients indicating that this regimen might be safe for patients with sufficient RKF. Zhang et al. (13.) reported similar results of slow decline of RKF in twice-weekly HD regimen, especially within the first year (OR = 7.2, 95% CI: 1.1–47.1). Fernandez-Lucas et al. (4) also implied that starting dialysis with a twice-weekly schedule might be an effective prescription to preserve RKF without compromising patient safety. Factors related to better preservation of RKF in twice-weekly HD may include extracellular fluid volume expansion, less inflammatory response and less kidney ischemia in twice-weekly HD if the treatment runs without complication (14).

Improvement of Vascular Access Longevity

It is reasonable to think that less frequent arteriovenous access cannulations may result in the improvement of vascular access longevity. Higher risks of vascular access events and vascular access-related hospitalization were found in daily HD patients compared with those in thrice-weekly HD patients (15). Fewer invasive procedures may cause fewer vascular access events where mechanisms of injury include vascular intimal injury, stenosis,

thrombosis, and infection. These are all important factors to consider as arteriovenous access function is independently associated with patient's long-term mortality, especially in those whose native vasculature is unfavorable, e.g., diabetics and the aged (16).

Improvement of Medical Resources Utilization

Obviously, twice-weekly HD schedule would provide more resources and chair-time availability for the ESRD populations to receive treatments versus the current resource allocation with thrice-weekly HD. In addition, the medical cost for twice-weekly HD patients may be substantially reduced at either the individual or the facility-based level. This would be beneficial for developing countries which may have limited medical resources. Even for developed countries, it is of great importance to effectively maximize the use of resources as well.

Higher Health-Related Quality of life

Spending shorter time on dialysis also allows a patient to have more time to engage in other activities, such as traveling, reading, etc., or even just spending time with their family. One less treatment can also allow the family member to save transportation time to and from the dialysis center. In addition, fewer dialysis treatments will reduce the burden of postdialysis fatigue. These advantages of twice-weekly HD potentially offer patients a much higher QOL (2,17,18). However, the DOPPS China cross-sectional study (1) did not show this benefit with similar QOL scores for twice-weekly and thrice-weekly HD in both physical and mental components. This may be due to the overall health-related quality of life which is also associated with many other factors, such as patients' age, comorbidities, treatment adequacy, and treatment complications.

Potential Unfavorable Effect of Twice-weekly Dialysis

Inadequacy of Dialysis

Dialysis dose is closely related to outcomes in the maintenance HD population (19,20). Although the NKF/KDOQI clinical practice guidelines recommended a minimum single pool Kt/V of 1.2 for thrice-weekly HD patients with little or no RKF and a minimum weekly standardized Kt/V (i.e., a combined weekly urea clearance by HD and RKF) of 2.1 (21), the dialysis dose for twice-weekly HD patients is supported by few compelling studies. In a prospective cohort study (22), the average weekly $spKt/V$ in patients on twice-weekly and thrice-weekly HD were 3.4 and 5.1, respectively. However, no association of higher $spKt/V$ with short-term mortality was found in twice-weekly HD (HR=0.6, 95% CI: 0.2–1.7, $p=0.7$).

An appropriate target dose of $spKt/V$ per session for twice-weekly HD is unknown. In a study from India (23), prolonging treatment time to increase $spKt/V$ could improve anemia, blood pressure, albumin, and QOL. In China, treatment duration in twice-weekly HD is generally longer in duration than that of thrice-weekly HD (253 ± 28 vs. 240 ± 17 minutes, $p < 0.05$) and patients on twice-weekly dialysis have a 6.8 times likelihood of being prescribed a session length of more than 240 minutes. However, not surprisingly, the $StdKt/V$ remained

lower in twice-weekly HD compared to thrice-weekly HD (1.45 ± 0.19 vs. 2.11 ± 0.26 , $p < 0.05$) (1).

To help determine an appropriate target of spKt/V for twice-weekly HD patients, we conducted a multicenter randomized controlled pilot study (registered at ClinicalTrials.gov as NCT00906555; unpublished data). A total of 163 twice-weekly HD patients from 17 dialysis centers were randomized into either the intervention or maintenance group. SpKt/V was increased to more than 1.70 in the intervention group by expanding dialyzer membrane area, prolonging treatment time, increasing blood flow, or dialysate flow rate. A higher StdKt/V (1.7 ± 0.1 vs. 1.6 ± 0.1) and spKt/V (1.9 ± 0.6 vs. 1.6 ± 0.2) were kept in the intervention group compared to the maintenance group over the 96-week follow-up. Although the overall survival between two groups were similar ($p = 0.58$), the 1 year major cardio-cerebrovascular events (MACE)-free survival in the intervention group was better than those in the maintenance group (84% vs. 77%, $p = 0.03$). SF-36 and higher physical function scores were also higher in the intervention group. Given the small sample size of this study, whether or not increasing dialysis dose could improve survival in twice-weekly HD patients remains to be proven in the future.

Malnutrition

The effect of HD frequency on nutrition remains uncertain. In a small observational study, nutrition status was compared between 23 patients undergoing twice-weekly HD and 51 patients undergoing thrice-weekly HD (12). After an 18-month follow-up, similar albumin, normalized protein catabolic rate (nPCR), cholesterol, phosphorus, and potassium were found between the two groups except for higher triglycerides in thrice-weekly HD patients. Similar findings were reported from Thailand in patients who received weekly Kt/V of over 3.6 (24). However, in the China DOPPS (1) and Huang's prospective cohort study (8), lower nPCR were found in the twice-weekly HD patients which might imply patients were under more strict protein restrictions or even were malnourished.

There are common recommendations that protein intake should be 0.6–0.8 g/kg/day and 1.0–1.2 g/kg/day, respectively, for predialysis and thrice-weekly HD patients. However, few reports investigated the dietary recommendation for patients on less frequent HD. Caria et al. (25) suggested very low protein and low phosphorus diets supplemented with ketoacids for once-weekly HD patients; Obi et al. (26.) proposed 0.8–1.0 g/kg/day dietary protein intake to twice-weekly HD patients with substantial RKF. The effects of dietary protein restriction with less frequent HD on patients' RKF, nutrition, mortality, and QOL need further investigation.

Anemia

For twice-weekly HD patients, the low HD frequency is beneficial by reducing the amount of blood loss. However, an inadequate dialysis dose may increase the accumulation of uremic toxin and lead to suppressed RBC production and low response to ESA in addition to the low frequency and low dose of ESA administration (12,13). Patients in China on twice-weekly HD had higher likelihood of $\text{Hgb} < 9$ g/dl (27). The reason was postulated as patients

on twice-weekly HD are more likely to have less insurance coverage and are less likely to meet dialysis adequacy targets compared with those on thrice-weekly HD (12).

Interdialytic Weight Gains and Intradialytic Hypotension

Higher interdialytic weight gains (IDWG) is assumed in twice-weekly HD regimen compared with thrice-weekly regimen. Consequently, a greater likelihood of intradialytic hypotension and cardiac complications would be expected due to more aggressive ultrafiltration requirements (28). However, this is not the case when patients can have their fluid balance properly controlled due to their substantial RKF or their intentional fluid restriction. The fluid removal in twice-weekly HD treatments can be similar (1) or even be a little bit lower compared with those in thrice-weekly patients, with similar (4) or fewer (12) hypotension episodes.

Nevertheless, we suggest those patients who have much greater IDWG and frequent intradialytic hypotension episodes avoid twice-weekly HD prescriptions even if a high spKt/V could be ensured. Intensified patient education and timely transition to thrice-weekly HD may be important. In China, patients on twice-weekly HD regimen usually receive longer treatments than thrice-weekly HD patients, which allows for a tolerable fluid removal rate that reduces the risk of hypotension. The balance of prolonging the treatment duration and increasing the frequency of treatment should be considered carefully. We sometimes find that patients' poor education on fluid restriction is the cause of large IDWGs and the requirement for more frequent dialysis treatments. However, more frequent treatments may also result in high IDWGs due to faster RKF loss and an unrestricted fluid intake. Thus, before patients are switched to frequent dialysis, education on fluid intake should be attended to first.

Electrolyte Imbalance

Electrolyte imbalance is another important factor when considering dialysis frequency. High risks of hospitalization and mortality were observed during long interdialytic intervals (29–31). However, it is still unclear if there are more electrolyte imbalances in patients with substantial RKF on twice-weekly HD and in which conditions patients on twice-weekly dialysis can maintain electrolyte balance. Adverse outcomes related to the long interdialytic interval have not been observed among those incident patients on twice-weekly HD with substantial RKF. Whether the potential benefits of preserving RKF in twice-weekly HD can counteract the potential risks of the long interval remains unknown (29). Moreover, electrolyte balance is associated with patient dietary intake, infection, and metabolism. Accordingly, dialysis frequency should be individually adjusted by monitoring the serum level of electrolyte.

Implementation of Twice-Weekly Dialysis

Considering the advantages and disadvantages of a twice-weekly HD regimen, the prescription of dialysis frequency should be decided according to the patient's individual situation. In a longitudinal study of 23,645 incident HD patients, Obi et al. found better preserved RKF in patients on an incremental regimen (starting dialysis with twice-weekly

HD) compared with matched patients receiving a conventional thrice-weekly HD regimen (11). Similar overall survival was found between the two HD regimens among the patients with substantial baseline RKF, but with a higher mortality risk in those with the incremental regimen without adequate baseline RKF. In addition, they found a trend toward lower mortality associated with the incremental regimen across higher RKF and lower IDWG. This study indicated that initiating twice-weekly HD regimen in incident patients may be a safe treatment regimen for preservation of RKF and may have a similar survival at least during the first year of dialysis if the patients have a substantial RKF. However, it should be noted that it was a nonrandomized study with potential selection bias, and increasing the dialysis dose over time by carefully monitoring the RKF reduction is suggested given the differential in mortality risks between the patients with and without RKF.

A recent paper by Kalantar-Zadeh et al. proposed 10 criteria for twice-weekly HD (Table 2) (17). Although further verification is needed regarding these criteria, they may be beneficial for nephrologists to consider in recommending twice-weekly dialysis as an option for patients who prefer, and are able to, initiate a low dose or incremental HD regimen. Urine output more than 0.5 l/day was considered to be a criterion that must be met when implementing twice-weekly HD. However, in a Chinese observational study (4), twice-weekly HD in anuric patients with >5 years of HD vintage showed significantly longer survival as compared to those thrice-weekly HD patients. This may indicate the importance of IDWG restriction rather than a specific value of urine output. Close monitoring of patients' fluid status, nutrition, anemia, and electrolyte balance will be helpful to determine the indications for transitioning from twice-weekly to thrice-weekly HD and then justifying the necessity of increasing the dialysis frequency over time.

In summary, based on the current small number of nonrandomized studies, the potential pros and cons of twice-weekly HD may depend on patients' RKF and other factors, including age, nutrition, comorbid conditions, self-management ability, medication adherence, medical, and finance resources. Prescriptions may need to be continually adjusted to meet the adequacy requirements for solute and fluid removal for patients on twice-weekly dialysis. Longer treatment times per session and the protein restriction may benefit those on twice-weekly HD as well. However, until now, there is little convincing evidence for which comorbid conditions are amenable and safe for starting twice-weekly HD and when patients should transition to more frequent HD regimens. A prudent patient selection and close dialysis adequacy monitoring may be necessary for this medical treatment choice. More randomized prospective controlled studies for the critical evaluation of twice-weekly dialysis are encouraged.

Acknowledgments

Yucheng Yan is supported by research grants from the National Nature Science Foundation of China (81470918).

References

1. Bieber B, Qian J, Anand S, Yan Y, Chen N, Wang M, et al. Two-times weekly hemodialysis in China: frequency, associated patient and treatment characteristics and Quality of Life in the China

- Dialysis Outcomes and Practice Patterns study. *Nephrol Dial Transplant*. 2014; 29(9):1770–1777. [PubMed: 24322579]
2. Rhee CM, Unruh M, Chen J, Kovesdy CP, Zager P, Kalantar-Zadeh K. Infrequent dialysis: a new paradigm for hemodialysis initiation. *Semin Dial*. 2013; 26(6):720–727. [PubMed: 24016197]
 3. Hanson JA, Hulbert-Shearon TE, Ojo AO, Port FK, Wolfe RA, Agodoa LY, et al. Prescription of twice-weekly hemodialysis in the USA. *Am J Nephrol*. 1999; 19(6):625–633. [PubMed: 10592355]
 4. Fernandez-Lucas M, Teruel-Briones JL, Gomis-Couto A, Villacorta-Perez J, Quereda-Rodriguez-Navarro C. Maintaining residual renal function in patients on haemodialysis: 5-year experience using a progressively increasing dialysis regimen. *Nefrologia*. 2012; 32(6):767–776. [PubMed: 23169359]
 5. Lin X, Yan Y, Ni Z, Gu L, Zhu M, Dai H, et al. Clinical outcome of twice-weekly hemodialysis patients in Shanghai. *Blood Purif*. 2011; 33(1–3):66–72. [PubMed: 22212562]
 6. Stankuviene A, Ziginiskiene E, Kuzminskis V, Bumblyte IA. Impact of hemodialysis dose and frequency on survival of patients on chronic hemodialysis in Lithuania during 1998–2005. *Medicina (Kaunas)*. 2010; 46(8):516–521. [PubMed: 20966627]
 7. Elamin S, Abu-Aisha H. Reaching target hemoglobin level and having a functioning arteriovenous fistula significantly improve one year survival in twice weekly hemodialysis. *Arab J Nephrol Transplant*. 2012; 5(2):81–86. [PubMed: 22612193]
 8. Hwang HS, Hong YA, Yoon HE, Chang YK, Kim SY, Kim YO, et al. Comparison of Clinical outcome between twice-weekly and thrice-weekly hemodialysis in patients with residual kidney function. *Medicine*. 2016; 95(7):e2767. [PubMed: 26886622]
 9. Wang AY, Lai KN. The importance of residual renal function in dialysis patients. *Kidney Int*. 2006; 69(10):1726–1732. [PubMed: 16612329]
 10. Termorshuizen F, Dekker FW, van Manen JG, Korevaar JC, Boeschoten EW, Krediet RT. Relative contribution of residual renal function and different measures of adequacy to survival in hemodialysis patients: an analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)-2. *J Am SocNephrol*. 2004; 15(4):1061–1070.
 11. Daugirdas JT, Greene T, Rocco MV, Kaysen GA, Depner TA, Levin NW, et al. Effect of frequent hemodialysis on residual kidney function. *Kidney Int*. 2013; 83(5):949–958. [PubMed: 23344474]
 12. Lin YF, Huang JW, Wu MS, Chu TS, Lin SL, Chen YM, et al. Comparison of residual renal function in patients undergoing twice-weekly versus three-times-weekly haemodialysis. *Nephrology*. 2009; 14(1):59–64. [PubMed: 19019171]
 13. Zhang M, Wang M, Li H, Yu P, Yuan L, Hao C, et al. Association of initial twice-weekly hemodialysis treatment with preservation of residual kidney function in ESRD patients. *Am J Nephrol*. 2014; 40(2):140–150. [PubMed: 25171342]
 14. Daugirdas JT, Bernardo AA. Hemodialysis effect on platelet count and function and hemodialysis-associated thrombocytopenia. *Kidney Int*. 2012; 82(2):147–157. [PubMed: 22592187]
 15. Suri RS, Larive B, Sherer S, Eggers P, Gassman J, James SH, et al. Risk of vascular access complications with frequent hemodialysis. *J Am SocNephrol*. 2013; 24(3):498–505.
 16. Park HS, Kim WJ, Kim YK, Kim HW, Choi BS, Park CW, et al. Comparison of outcomes with arteriovenous fistula and arteriovenous graft for vascular access in hemodialysis: a prospective cohort study. *Am J Nephrol*. 2016; 43(2):120–128. [PubMed: 27022896]
 17. Kalantar-Zadeh K, Unruh M, Zager PG, Kovesdy CP, Bargman JM, Chen J, et al. Twice-weekly and incremental hemodialysis treatment for initiation of kidney replacement therapy. *Am J Kidney Dis*. 2014; 64(2):181–186. [PubMed: 24840669]
 18. Kalantar-Zadeh, Kamyar, Casino, Francesco G. Let us give twice-weekly hemodialysis a chance: revisiting the taboo. *Nephrol Dial Transplant*. 2014; 29(9):1618–1620. [PubMed: 24782534]
 19. Depner T, Daugirdas J, Greene T, Allon M, Beck G, Chumlea C, et al. Hemodialysis Study Group: dialysis dose and the effect of gender and body size on outcome in the hemo study. *Kidney Int*. 2004; 65(4):1386–1394. [PubMed: 15086479]
 20. Port FK, Wolfe RA, Hulbert-Shearon TE, McCullough KP, Ashby VB, Held PJ. High dialysis dose is associated with lower mortality among women but not among men. *Am J Kidney Dis*. 2004; 43(6):1014–1023. [PubMed: 15168381]

21. National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. *Am J Kidney Dis.* 2015; 66(5):884–930. [PubMed: 26498416]
22. Panaput T, Thinkhamrop B, Domrongkitchaiporn S, Sirivongs D, Praderm L, Anukulanantachai J, et al. Dialysis dose and risk factors for death among ESRD patients treated with twice-weekly hemodialysis: a prospective cohort study. *Blood Purif.* 2014; 38(3–4):253–262. [PubMed: 25573488]
23. Chauhan R, Mendonca S. Adequacy of twice weekly hemodialysis in end stage renal disease patients at a tertiary care dialysis centre. *Indian J Nephrol.* 2015; 25(6):329–333. [PubMed: 26664206]
24. Supasyndh O, Satirapoj B, Seenamngoen S, Yongsiri S, Choovichian P, Vanichakarn S. Nutritional status of twice and thrice-weekly hemodialysis patients with weekly Kt/V > 3.6. *J Med Assoc Thai.* 2009; 92(5):624–631. [PubMed: 19459522]
25. Caria S, Cupisti A, Sau G, Bolaso P. The incremental treatment of ESRD: a low-protein diet combined with weekly hemodialysis may be beneficial for selected patients. *BMC Nephrol.* 2014; 15:172. [PubMed: 25352299]
26. Obi Y, Eriguchi R, Ou S, Rhee CM, Kalantar-Zadeh K. What is known and unknown about twice-weekly hemodialysis. *Blood Purif.* 2015; 40(4):298–305. [PubMed: 26656764]
27. Zuo L, Wang M, Hou F, Yan Y, Chen N, Qian J, et al. Anemia management in the China dialysis outcomes and practice patterns study. *Blood Purif.* 2016; 42(1):33–43. [PubMed: 27045519]
28. Foley RN, Herzog CA, Collins AJ. United States Renal Data System: blood pressure and long-term mortality in United States hemodialysis patients: USRDS Waves 3 and 4 Study. *Kidney Int.* 2002; 62(5):1784–1790. [PubMed: 12371980]
29. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced cardiac injury: determinants and associated outcomes. *Clin J Am Soc Nephrol.* 2009; 4(5):914–920.
30. Shoji T, Tsubakihara Y, Fujii M, Imai E. Hemodialysis-associated hypotension as an independent risk factor for two-year mortality in hemodialysis patients. *Kidney Int.* 2004; 66(3):1212–1220. [PubMed: 15327420]
31. Flythe JE, Kimmel SE, Brunelli SM. Rapid fluid removal during dialysis is associated with cardiovascular morbidity and mortality. *Kidney Int.* 2011; 79(2):250–257. [PubMed: 20927040]
32. Obi Y, Streja E, Rhee CM, Ravel V, Amin AN, Cupisti A, et al. Incremental hemodialysis, residual kidney function, and mortality risk in incident dialysis patients: a cohort study. *Am J Kidney Dis.* 2016; 68(2):256–265. [PubMed: 26867814]

TABLE 1

Potential effects of twice-weekly hemodialysis regimen on patient's outcome compared with that of thrice-weekly hemodialysis

Favorable effect	Unfavorable effect
Preservation of RKF	Inadequate dialysis dosage
Improvement of vascular access longevity	Diet restriction and malnutrition
Effective utilization of medical resources	Anemia
Higher health-related quality of life	IDWG and intradialytic hypotension Electrolyte imbalance

RKF, residual kidney function; IDWG, interdialytic weight gain.

TABLE 2Proposed criteria for twice-weekly hemodialysis^a

1	A urine output 0.5l/day
2	Inter-dialytic fluid gain < 2.5 kg or <5% of dry weight
3	Limited or readily manageable cardiovascular or pulmonary symptoms without clinically significant fluid overload
4	Appropriate body size
5	Infrequent or readily manageable hyperkalemia
6	Infrequent or readily manageable hyperphosphatemia
7	Good nutritional status without overt hypercatabolic state
8	Appropriate responsiveness to anemia therapy with hemoglobin >8 g/dl
9	Limited or easily manageable comorbid conditions
10	Satisfactory quality of life

^aAdapted from Kalantar-Zadeh et al¹⁷.