Supplement 11| External Review Results and Reflection

Overall evaluation of guideline development			
Field (item)		Review Opinion	Reflection of revision
Necessity of developing treatment guidelines and appropriateness of development planning		Most of the key questions are basic in clinical practice, and it is expected that centers that are applying to existing treatments will receive firm support through evidence, and hospitals that have not been implemented will be able to apply them to clinical practice based on guidelines. In the future, it is necessary to expand various medical guidelines (dialysis blood vessel management, drug treatment, nutritional approach, etc.) and collaborate with a group of experts in this regard.	Not applicable
Methodological rigor in guideline development		Searching for evidence and drawing conclusions using it does not seem to be a big problem. However, if the level of evidence for widely known information in clinical practice is low, or if the level of evidence for questionable content is high, treatment may be confused. It seems that a special comment from the guideline development group on this is necessary.	The process of deriving the recommendation grade and level of evidence for each recommendation is described in detail, and the advantages and disadvantages of clinical application are described.
Reasonability of making recommendations		There is no doubt about the rationality of the recommendation decision. It is a basic content about implementing treatment based on evidence, and will be helpful in practical clinical practice.	Not applicable
Degree of consent and usability of guidelines		Overall, I agree with the treatment guidelines. However, the content of the key questions is lacking, and I think that measures are needed to spread the medical guidelines.	The process of discussing additional key questions in the revision plan of the medical guidelines is described, and the expansion plan is described in the text.
Evaluation of individual recommendations			
Topic	No.	Review Opinion	Reflection of revision
All recommendations		Each item in the advisory considerations is consistently well structured. However, the titles of benefits and harms, patient values and preferences, obstacles and facilitators, overcoming measures, and resources are a little difficult to come by. Isn't there an easier and more refined title?	Each item of the medical guidelines was maintained in principle as it was in accordance with the guidelines for writing the medical guidelines.
		We asked for opinions on how to express the expert consensus recommendation with E.	Since the expert consensus has no level of evidence, it was kept as it is to avoid misunderstandings.
		When writing the PICO, it would be better to put the position of the last (O) in front of the question mark (?). […] … Is there any prognosis improvement effect? (O)]	We tried to eliminate misunderstandings by presenting the PICO items in the

		rather than [… .., etc. Is there an effect of improving the prognosis (O)?] It seems that the English 'O' will not be misunderstood as the circled 'O'.	form of a table.
Start of HD	1.1.	Prior to the start of hemodialysis, it would be good if there were information on patient education methods for selecting the dialysis method, the period of education, and the preservation of blood vessels.	Since it falls outside the key question, we will consider it when revising the recommendations in the future.
	1.1.	I would like to see the addition of the GFR for the CKD G5.	The GFR was additionally indicated.
	1.2.1.	I hope that it is explained in an easy-to-understand manner as 'It is recommended to prepare a dialysis vessel in advance to avoid central venous catheter insertion before hemodialysis'.	According to the opinion, the recommendation was changed to "We recommend that preparation of arteriovenous access prior to hemodialysis initiation to avoid central venous catheter insertion."
	1.2.	No mention is made of an appropriate time for preparation of AVF (or AVG) prior to dialysis. Ex) GFR 15~20 mL/min, rapid GFR decrease of 10 mL/min/year, etc.	According to the opinion, the following content was added to the summary of evidence and references were inserted. "There is no direct evidence data on the timing of the referral for AVF (AVG) formation creation, but the recent KDOQI vascular access guidelines show that CKD G5-ND is characterized by a gradual decrease in renal function. Expert opinions were presented that it is reasonable to evaluate the blood vessels and request surgery when the GFR is 15-20 mL/min/1.73 m^2 in CKD patients. The guidelines also published recommendations at the level of expert opinion that patients with CKD G5-ND should be referred early when their condition is unstable and the GFR is rapidly decreasing (e.g., >10 mL/min/year). This is based on values from well-conducted simulation studies."
	1.2.	In addition to mortality, the pre-generation of vascular access in CKD G5-ND requires evaluation of other benefits, such as improvement	The key question reviewed in this guideline is "In adult CKD G5 patients, does the preparation of vascular

		of eGFR.	access prior to the initiation of dialysis improve post-dialysis patient survival, compared to non-preparation of vascular access?", the clinical evidence for other clinical indicators has not been reviewed. It is expected that this will be supplemented in the follow-up guidelines.
Frequency and dose of HD	2.1.	If residual renal function remains, it would be nice to have information on the evaluation method for residual renal function and the frequency of dialysis.	The evaluation method of residual renal function will be considered in a later revision.
	2.1.	If the definition of 'residual renal function' is further described, the meaning seems to be clearer.	The definition of residual renal function has been additionally described. "Usually, residual renal function is measured by collecting urine. If the daily urine volume is less than 100cc, it is judged that there is no residual renal function."
	2.1.	Is the definition of no residual renal function considered as GFR=0? What other factors can be used to determine that an appropriate dialysis is being performed when the actual dialysis time and frequency are reduced?	The definition of residual renal function has been additionally described. Other elements of appropriate dialysis will be considered in future revisions.
	2.1.	Various situations that can be seen in clinical practice, recommendations for treatment for 4 hours 2 times a week or 3 hours 3 times a week treatment, etc.	Described in patient values and preferences. If the life expectancy is less than 6 months, conservative treatment is necessary and if the patient requests it, dialysis can be tried twice a week or for less than 4 hours per session.
	2.2.	The recommendation only recommended keeping the target dialysis adequacy at spKt/V 1.4, but it would be good to present the dialysis adequacy that must be met at least like the K/DOQI guideline. If only the target dialysis adequacy is presented, the HIRA's dialysis adequacy evaluation standard will be upgraded from the	The minimum requirement of spKt/V is additionally described.

		current spKt/V 1.2 to 1.4 after this guideline is distributed, thereby causing unintended damage to frontline medical institutions. Looking at the evidence table 12 presented in the recommendation, it is suggested that there is no statistically significant difference in hazard ratio between spKt/V 1.2-1.4 and 1.4-1.6, so it is not unreasonable to present the minimum requirement together.	
	2.2.	Description of the dangers of excessively high spKt/V	Same as above
Dialysis membrane and modality for HD	3.1.2.	In 3.1.1, high-flow hemodialysis is recommended for hemodialysis patients, but in 3.1.2, is it necessary to recommend high-flow hemodialysis in some patient groups?	3.1.2 was deleted and unified into one recommendation.
	3.1.2.	Instead of the period of 3.7 years or more, it would be better to specify 3 years and several months in an easy-to-understand way for general patients. Also, when describing such a period, it seems that it may give vague fear to the dialysis patient that he or she has been on dialysis for a long time and must change to a method other than the existing dialysis method.	Same as above
	3.2.2.	The guideline mentioned the need for health insurance coverage of online HDF. For this, it is necessary to present a standard at the level of expert consensus. (e.g. hyperphosphatemia, dialysis-related amyloidosis, cardiovascular risk)	The discussion on online HDF health insurance coverage is beyond the scope of the core question, and if future research is published, it will be considered in a later revision.
	3.2.	We generally agree with recommendations made on the basis of evidence in accordance with scientific methodologies. However, when it comes to hemodiafiltration therapy (online HDF), there are some drawbacks. Above all, it is regrettable that recently published studies were excluded as the basis for drawing conclusions. In particular, it has been found that the effect of improving the survival rate of patients is due to the high-volume HDF rather than the online HDF itself. Based on these findings, the NICE guideline published in 2018 recommended that “in case of initiating dialysis in a hospital, select HDF rather than HD” (see below). However, studies supporting this are excluded from the analysis for evidence in this guideline. In the end, it can be said that the recommendation is based on the evidence at least at the time of the publication of the ESHOL study (2103) for online HDF. So, if you can fix it now, it	Added the following to the recommended considerations. Online HDF is a dialysis method that is advantageous for solutes removal by diffusion and convection, but additional large-scale prospective clinical studies are needed to prove the effect of improving various clinical indicators. Recommendations may be changed depending on the future results of one RCT currently in progress.

		looks like it needs to be fixed.	
	3.2.	Comparison with new treatments such as on-line HDF as well as various filters and theranova.	Research on online hemodiafiltration filters is currently insufficient, so if future research is published, it will be considered in a later revision.
	3.2.1.	How about adding the contents of the underlined sentences below to the existing recommendations In addition, it would be good to add explanations and supporting studies to the summary of evidence. “Online HDF did not differ in all mortality, cardiovascular mortality, hospitalization rates and quality of life compared to high-flow hemodialysis. However, there is evidence that high-volume on-line HDF improves patient survival.	Added the following to the recommended considerations. Online HDF is a dialysis method that is advantageous for solutes removal by diffusion and convection, but additional large-scale prospective clinical studies are needed to prove the effect of improving various clinical indicators. Recommendations may be changed depending on the future results of one RCT currently in progress.
	3.2.2.	In the existing recommendation, it is proposed to replace high-efficiency online HDF with high-volume HDF. Considering cost/effectiveness, high-efficiency online HDF may be considered. → Considering cost/effectiveness, high-volume online HDF may be considered.	The expert consensus was described as follows. Considering cost/effectiveness, high-volume online HDF may be considered.
Anticoagulant therapy of HD	4.1.	If the risk of bleeding is not high, UFH is recommended as a standard treatment, but shouldn't it be said that LMWH can be considered in consideration of cost/effectiveness or according to the judgment of the medical staff in a similar meaning to HDF?	As mentioned in <Other Considerations>, it was determined that it is difficult to strongly recommend LMWH as a standard treatment because the overall level of evidence of the studies conducted to date is low. Instead, it was clarified that it is a treatment that can replace standard treatment, and when it is replaced, the medical condition of the individual patient (type of comorbidity, medications being used, etc.) and cost-effectiveness are taken into account.
	4.1.	Differences depending on the patient's individual	Same as above

		disease type and medication being taken.	
Volume and fluid status in HD patients	5.1.	Agree on the risk of overhydration. Comparison required for >4%, >5%, >7%, or >10% or more for increased risk of overweight.	Although most of the results are observational studies, in most studies, the higher the IDWG, the poorer the prognosis. (Refer to the table of evidence in the text)
	5.1.1.	The 4% standard is difficult to apply clinically to both medical staff and patients. Even if the research results are like this, it is not easy to apply these figures to the additional description, so it would be helpful for clinical practice to give an expert opinion around 5%.	The Japanese JSDT CPG was supposed to limit it to 5%, and at the same time UFR per hour was also presented in the guidelines. This reflects a longer dialysis time than Korea, and it is difficult to apply the Japanese standards to Korea as the dialysis environment is different from Korea. It will be a standard compiled based on domestic research. I would appreciate it if you could understand it as a standard value suggested for education to patients.
	5.1.2.	It would be better to have information on how to evaluate excess body fluids or dry weight and how often.	We will consider adding it to our future update guidelines.
	5.1.2.	"2. Patients whose predialysis weight exceeds 4% of their dry weight can be assessed for excess fluid volume and considered for dietary compliance, nutritional status assessment, and dietary education." It would be better to delete the phrase "Evaluation of nutritional status" from the recommendation, as it conflicts with "Evaluation of nutritional status should be considered for patients with low liver weight gain."	We appreciate your understanding that this means that patients who gain excessive weight between dialysis should consider diet through nutritional status evaluation, and patients with low weight gain should evaluate whether they have adequate nutritional intake. Thanks for the review.
	5.2.	In line 13 from the top of the Summary of Evidence, "Recently, Dunlop et al. reported that low-sodium dialysate (Na <138 mEg/L), medium-concentration (Na 138-140 mEg/L) and high-concentration sodium dialysate (Na <140 mEq/L) were used. A comparative meta-analysis was published and reported that the use of low-sodium dialysate could increase hypotension and body weight during dialysis compared to the intermediate concentration [12]. There was less weight gain when low sodium dialysate was used." Conflicts. It looks like it needs confirmation.	We have made corrections to your comments.

Blood pressure control in HD patients	6.1.	4) If you look at the resource, the bottom line says, “There is currently no place in Korea that provides a 44-hour portable blood pressure monitor.” It is necessary to check whether the 44 hour is a typo or the 44 hour is correct.	44 hours is correct.
	6.1.	Whether the BP is an office BP or a home BP. Is it based on 24hr BP monitoring or is it a one-time BP?	All references to BP in the literature except for ambulatory BP are office BP (dialysis unit BP).
	6.1.1.	We agree with the recommendations stated in the recommendations as it is very difficult to set an appropriate blood pressure target in hemodialysis patients. However, I would like to discuss the results of the related research in the summary of the evidence. In addition, 5.1. the main background of the recommendation to not exceed 4% in weight gain between dialysis was based on the results of a domestic study, and the study was based on CRC for ESRD data analysis. In 6.1., There were domestic data on optimal blood pressure, and it was a thesis based on CRC for ESRD data analysis. In addition to wishing for more detailed information on this, I would like to suggest that it would be of great help if you could mention a little more about the optimal blood pressure, measurement time, and method, which would be suggested as expert consensus recommendations.	The recommendation reflects the lack of RCT evidence, and the analysis of observational studies is at a lower level of evidence, so it is difficult to induce a change in the recommendation. Reflecting the review opinions, the details of domestic observational studies and overseas observational studies have been introduced in more detail as follows. We will do our best to present detailed information such as measurement time and method in the follow-up treatment guidelines.
Evaluation and monitoring of HD patients	7.1.1.	I do not agree with the reason why the 3-month dialysis adequacy test cycle is recommended. Most global guidelines recommend a one-month cycle, and also in Korea, the current cycle of dialysis adequacy testing in the certification evaluation of the HIRA is set on a monthly basis. In terms of cost, the dialysis adequacy test is a low-cost test, so there is no cost obstacle to monthly testing.	Referring to the adequacy evaluation criteria of the Korean Society of Nephrology and the HIRA, ‘at least 6 months’ is indicated. For euphemism, the word ‘at least’ was added.
	7.1.	As for the recommendation of regular examination items and cycles for appropriate dialysis, it would be better to present a very euphemistic recommendation standard because the recommendation grade is expert consensus recommendation and the level of evidence is 'low'.	Same as above
	7.1.4.	Since the KDIGO guidelines recommend HCV testing every 6-12 months, shouldn’t “at least” be omitted from the 6-month screening cycle? Would it be appropriate to have an ECG test cycle “at least” every 6 months?	In the 2018 KDIGO guideline, ‘every six months’ is indicated, and ‘at least six months’ is indicated by referring to the adequacy evaluation criteria of the

			Korean Society of Nephrology and the HIRA. The guideline has been inserted as a reference in the 'Summary of Evidence' section.
Non-standard setting of HD (elderly, children)	8.1.	Even if each paper is different, it is judged that the definition (age, etc.) of the elderly patient according to the domestic standard needs to be established to some extent.	Since the definition of the elderly is different for each study and there are not many domestic studies, the average age of the patients who participated in the studies included in the synthesis of evidence in this recommendation was recorded. As a domestic multicenter study on elderly patients with end-stage kidney failure is ongoing, it is considered that the results of domestic studies should be paid attention to.
	8.1.2.	How about deleting 'active' from the expression 'active conservative treatment' in Recommendation 2? In a situation where there are no clear guidelines for conservative treatment, it is ambiguous what the expression 'active' means and what does not mean 'active' conservative treatment.	The word 'active' in the recommendation has been deleted. Thanks for the review.