

Baxter

CHANGE ONE THING.

CHANGE EVERYTHING.




**INTRODUCING THERANOVA FOR
EXPANDED HEMODIALYSIS [HDx]**


HDx Clinical Evidence Series 2

- Economic Benefits
- Cardiovascular Outcomes

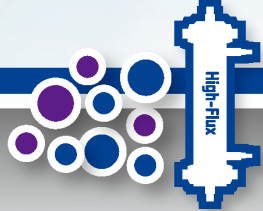
THERANOVA를 통한 확장된 혈액투석 : NOW IS THE TIME TO CHANGE EVERYTHING



중/대분자(500-45,000 Da) 요독소는 염증, 심혈관질환 (Cardiovascular disease, CVD) 및 기타 투석 관련 동반 질환의 발생과 관련이 있습니다.¹⁻³




심혈관질환은 염증, 죽상동맥 경화증 및 석회화와 연관성이 있습니다. 신부전(Kidney failure) 환자의 약 50%가 심혈관질환으로 사망합니다.⁴⁻⁶




기존의 고유량 투석막은 중/대분자 요독소 (최대 45,000 Da)의 제거에 제한적입니다.⁷

CHANGE ONE THING.


혈액투석 (HD)의 차세대 투석막, **Theranova**는 기존 HD 방식 대비 염증 및 심혈관질환과 관련된 중/대분자 (최대 45,000 Da) 제거율을 개선하여 정상 신장 기능에 한층 더 가까워졌습니다.^{3,8-11}



Theranova 투석막의 차별화된 디자인은 고유량 투석막에 비해 중/대분자(최대 45,000 Da)를 효과적으로 제거하는 동시에 필수 단백질을 선택적으로 유지하고 알부민 수치를 안정적으로 유지합니다.^{2,3,8-10,12,13}



후향적 분석(n=81) 결과, HDx 요법은 입원 일수 및 센터 내 약제 사용을 크게 감소시켰습니다.¹⁴ 무작위 대조 연구(n=171)에서 all-cause hospitalization이 43% 감소한 것으로 나타났습니다.¹⁵ 일부 환자에서는 특정 염증 지표의 개선이 관찰되었습니다(n=41).¹⁶



HDx 요법은 환자의 증상부담, 하지불안증후군(Restless leg syndrome), 요독성 소양증(Uremic pruritus) 및 투석 회복 시간 등 환자가 보고한 신질환 관련 삶의 질 결과를 개선할 수 있습니다.^{8,9,17,18}

CHANGE EVERYTHING.

투석막 하나를 변경하여 혈액투석 치료 결과들의 많은 부분을 바꿀 수 있습니다.¹⁰



Q.

선생님의 혈액투석 환자에게
경제적 이점 및 **심혈관 위험**을 고려할 때,
기존 HD Therapy에 대한 치료적 대안은 무엇일까요?

Economic
Benefits



Cardiovascular
Outcomes





Economic Benefits

Theranova를 통한 확장된 혈액투석(HDx)은 신부전 환자에서 입원, 감염 및 철분제 및 ESA와 같은 보조 약물의 사용을 감소시킵니다.¹⁹⁻²²

> Study 1

An initial evaluation of expanded hemodialysis on hospitalizations, drug utilization, costs, and patient utility in Colombia.

Ariza JG, et al. Ther Apher Dial. 2021;1-7.

✔ Study design

- Retrospective study
- Data from Renal Care Services medical records database in Colombia from 2017 to 2019 (N=81)
- To evaluate expanded hemodialysis on hospitalizations, drug utilization, costs, and patient utility

✔ Data included

- Demographic characteristics, comorbidities, years on dialysis, hospitalizations, medication use, and quality of life measured by the 36 item and Short Form versions of the Kidney Disease Quality of Life survey at the start of HDx, and 1 year after HDx

HDx 환자의 경우, 연간 입원 일수 및 ESA, 철분제, 고혈압 약제, 인슐린과 같은 주요 약물의 사용 용량에서 HF-HD 환자 대비 유의한 감소를 보였습니다.¹⁹

Hospitalizations and medication utilization with HF-HD or HDx¹⁹

| Outcome | HF-HD mean (95% CI), n=81 | HDx mean (95% CI), n =81 |
|--|----------------------------|----------------------------|
| Yearly hospitalization days | 5.94 (5.41-6.50) | 4.41 (3.97-4.90)* |
| Dosage per patient per year of ESA in international units | 181 318 (151 647- 210 988) | 168 124 (138 452-197 794)* |
| Dosage per patient per year of iron in milligrams | 959 (760-1158) | 759 (560-958)* |
| Dosage per patient per year of insulin in international units | 5383 (3274-7490) | 3434 (1327-5543)* |
| Number of tablets per patient per year of hypertension medications | 1183 (970-1394) | 731 (518-943)* |

*Statistically significant difference found in corresponding univariate GLM analysis of outcome on HDx. All had a P-value <0.01.

Clinics included had switched all patients from HF-HD to HDx and had at least a year of data on HF-HD and HDx. Generalized linear models were run on the outcomes of interest with an indicator for being on HDx. Annual cost estimates were also constructed.

CI=confidence interval; ESA=erythropoietin stimulating agent; HDx=expanded hemodialysis; HF-HD=high flux hemodialysis



Economic Benefits



Theranova를 통한 확장된 혈액투석(HDx)은 신부전 환자에서 입원, 감염 및 철분제 및 ESA와 같은 보조 약물의 사용을 감소시킵니다.¹⁹⁻²²

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HDx 치료 환자에서 비용 추정치 분석 결과, HF-HD 치료 환자 대비 연간 입원 비용은 약 24%, 약물 관련 비용은 약 7%~33% 낮았습니다.¹⁹

Annual costs with HDx and HF-HD¹⁹

| Annual per patient cost category | Percent change, HDx vs. HF-HD |
|----------------------------------|-------------------------------|
| Hospitalizations | -23.9% |
| ESA | -7.27% |
| Iron | -20.83% |
| Insulin | -32.64% |
| Antihypertensives | -30.16% |

Clinics included had switched all patients from HF-HD to HDx and had at least a year of data on HF-HD and HDx. Generalized linear models were run on the outcomes of interest with an indicator for being on HDx. Annual cost estimates were also constructed.

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> Study 2

Effectiveness of medium cut-off vs high flux dialyzers: A propensity score matching cohort study.

Molano-Triviño A, et al. Nephrol Dial Transplant. 2021;36(Supplement_1):gfab100-005.

✔ Study design

- Observational, multicenter retrospective cohort analysis
- To evaluate clinical effectiveness of HDx vs. HF-HD
- N=1098 (564 HDx, 534 HF-HD)
- Follow-up until 2 years

✔ Study objectives

- Hospitalization rate and duration, cardiovascular event rate, survival in a HD prevalent cohort in Colombia

HDx 환자군에서 HF-HD 환자군 대비 입원율은 18% 낮았으며, 입원의 주요 원인은 심뇌혈관 질환이었습니다.²⁰

Cardiovascular and Hospitalization events
(Negative binomial regression with weighted sample)²⁰

| | Estimate | 95% CI | P-value |
|-------------------------------|-------------|------------------|-------------|
| Cardiovascular events | | | |
| Rate per patient-year | | | |
| HF-HD | 0.27 | 0.20-0.33 | |
| HDx | 0.17 | 0.14-0.21 | |
| Incidence rate ratio | 0.65 | 0.47-0.91 | 0.01 |
| Hospitalization events | | | |
| Rate per patient-year | | | |
| HF-HD | 1.10 | 0.95-1.25 | |
| HDx | 0.90 | 0.80-1.00 | |
| Incidence rate ratio | 0.82 | 0.69-0.98 | 0.03 |

Adult Prevalent HD patients (> 90 days in HD) at Baxter Renal Care Services Colombia were included between September 1st, 2017 to November 30th, 2017. Weighted incidence rate ratios (IRRs) and rates and duration of hospitalization and cardiovascular events according to dialyzer type were obtained using binomial negative regression with the weighting sample. 1098 patients (37.7% women) were evaluated: 534 in HF-HD vs 564 in HDx, median age was 60.6 years. Mean time on HD was 5.6 years (SD 5.51) for HF-HD and 5.88 for HDx (SD 5.48).

CI=confidence interval; HD=hemodialysis; HDx=expanded hemodialysis; SD=standard deviation; HF-HD=high flux hemodialysis



Economic Benefits



Theranova를 통한 확장된 혈액투석(HDx)은 신부전 환자에서 입원, 감염 및 철분제 및 ESA와 같은 보조 약물의 사용을 감소시킵니다.¹⁹⁻²²

> Study 3

Effects of a medium cut-off (Theranova®) dialyser on haemodialysis patients: a prospective, cross-over study.

Cozzolino M, et al. Clin Kidney J. 2019 Nov 11;14(1):382-389.

✔ Study design

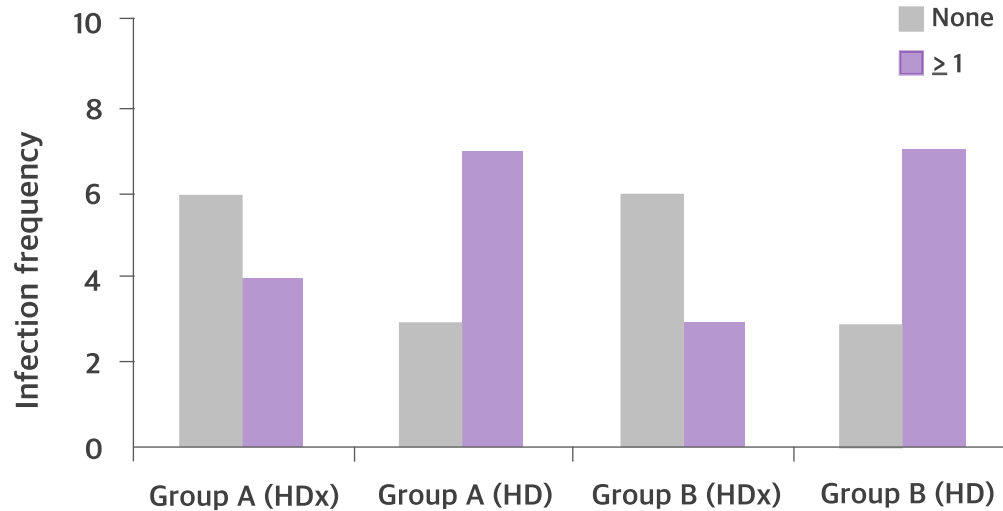
- Prospective, open-label, controlled, cross-over pilot study
- N=20 (10 HDx, 10 HF-HD)
- To evaluate effects of a MCO dialyser on HD patients
- Group A: 3 months HDx, then switched to 3 months HF-HD
- Group B: 3 months HF-HD, then switched to 3 months HDx

✔ Clinical outcome measures

- Hematochemical values, inflammatory markers, parameters of dialysis adequacy, incidence of adverse events, incidence of infections, number and causes of hospitalization

HDx 치료 환자에서 HF-HD 치료 환자 대비 총 감염 발생률이 낮았습니다 (n=7/19 vs n=14/20; P=0.03).²¹

Frequency of infections in Groups A and B following HD and HDx treatments^{21,*}



*Patients in Group A were treated with Theranova dialyser (HDx) for the first 3 months of the study, and then switched to conventional bicarbonate dialysis for the remaining 3 months. Patients in Group B were treated with bicarbonate dialysis for the first 3 months of the study, and then switched to HDx for the next 3 months.

Cross-over pilot study to compare HDx (novel MCO membrane Theranova® 400) and conventional HD in 20 prevalent HD patients. Biochemical, dialysis adequacy and safety measures were recorded. Ten patients underwent conventional HD high-flux dialyser and 10 patients underwent HDx for 3 months, and the patients then switched and received the other treatment for a further 3 months.

HD=hemodialysis; HDx=expanded hemodialysis; HF-HD=high flux hemodialysis; MCO=medium cut-off



Economic Benefits



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> Study 4

Medium cut-off dialyzer improves erythropoiesis stimulating agent resistance in a hepcidin-independent manner in maintenance hemodialysis patients: results from a randomized controlled trial.

Lim JH, et al. Sci Rep. 2020 Sep 29;10(1):16062.

Study design

- Post-hoc analysis of original RCT evaluating the effectiveness of MCO dialyzer on QoL (vs. HF dialyzer)
- To compare the ESA resistance between MCO and high-flux HD patients
- N=49 (24 HDx, 25 HF-HD)
- 12 weeks study period

Study endpoints

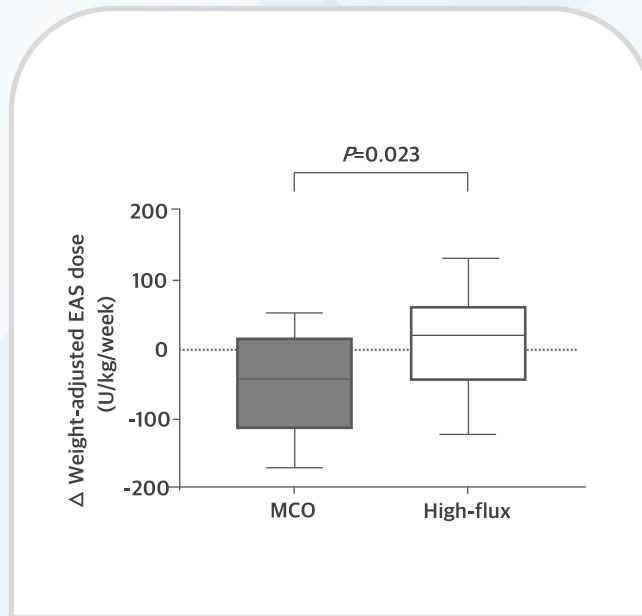
- Primary endpoints: changes of ERI between baseline and 12 weeks of treatment
- Secondary endpoints: iron- and anemia-related markers, reduction ratios of the iron regulator (hepcidin), inflammatory cytokine (TNF- α) at baseline and 12 weeks of treatment

Chronic maintenance HD patients treated with high-flux dialyzer at the Kyungpook National University Hospital were enrolled from July 2018 and followed up for 12 weeks. Forty-nine patients who underwent high-flux HD were randomly allocated to the MCO or high-flux group.

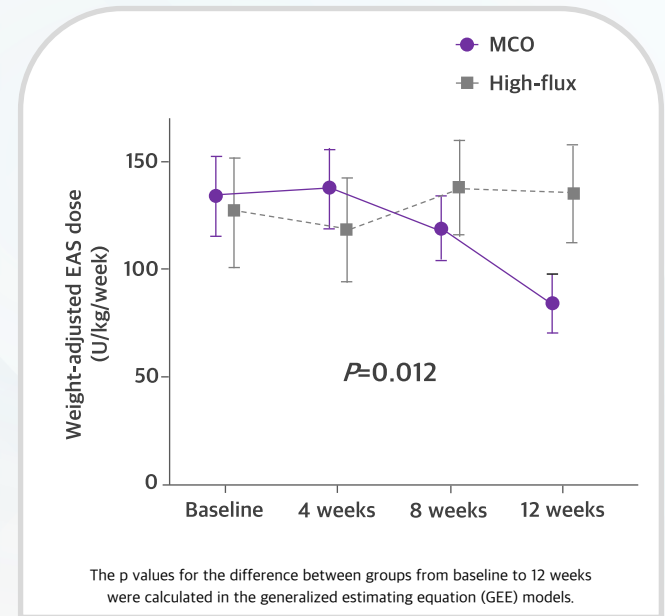
ESA=erythropoiesis stimulating agent; ERI=erythropoietin resistance index; HD=hemodialysis; HDx=expanded hemodialysis; HF-HD=high flux hemodialysis; MCO=medium cut-off

12주 차 HDx 치료 환자에서 weight-adjusted ESA 용량이 HF-HD 치료 환자 대비 유의하게 낮았습니다.²²

Comparison of weight-adjusted ESA²²



Serial changes in weight-adjusted ESA²²



The p values for the difference between groups from baseline to 12 weeks were calculated in the generalized estimating equation (GEE) models.



Cardiovascular Outcomes



Theranova를 통한 확장된 혈액투석(HDx)은 심혈관 질환 발생률을 낮출 수 있습니다.²⁰

> Study 2

Effectiveness of medium cut-off vs high flux dialyzers: A propensity score matching cohort study.

Molano-Triviño A, et al. Nephrol Dial Transplant. 2021;36(Supplement_1):gfab100-005.

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- Observational, multicenter retrospective cohort analysis
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- N=1098 (564 HDx, 534 HF-HD)
- Follow-up until 2 years

✔ Study objectives

- Hospitalization rate and duration, cardiovascular event rate, survival in a HD prevalent cohort in Colombia

HDx 환자군에서 HF-HD 환자군 대비, 심혈관 질환 발생률이 35% 낮았습니다.²⁰

Cardiovascular and Hospitalization events (Negative binomial regression with weighted sample)²⁰

| | Estimate | 95% CI | P-value |
|-------------------------------|-------------|------------------|-------------|
| Cardiovascular events | | | |
| Rate per patient-year | | | |
| HF-HD | 0.27 | 0.20-0.33 | |
| HDx | 0.17 | 0.14-0.21 | |
| Incidence rate ratio | 0.65 | 0.47-0.91 | 0.01 |
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CI=confidence interval; HD=hemodialysis; HDx=expanded hemodialysis; HF-HD=high flux hemodialysis; SD=standard deviation



Cardiovascular Outcomes



Online-HDF의 사용이 어려운 클리닉의 경우, 기존의 HD 치료 환자에서 HDx는 QoL 및 cardiovascular outcome 개선을 위한 치료적 대안이 될 수 있습니다.²³

> Study 5

Cardiovascular risk comparison between expanded hemodialysis using Theranova and online hemodiafiltration (CARTOON): A multicenter randomized controlled trial.

Lee Y, et al. Sci Rep. 2021;11(1):10807.

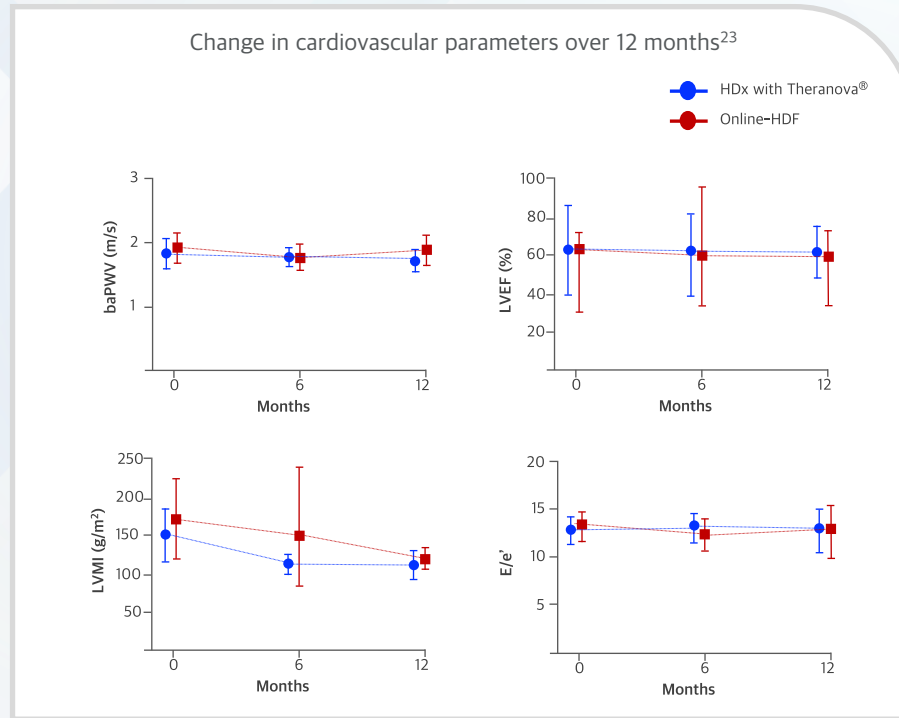
✔ Study design

- Multicenter, prospective, open-label, randomized trial
- To compare cardiovascular parameters (HDx vs. online-HDF)
- N=80 (43 HDx, 37 online-HDF)
- 1 year study period

✔ Study endpoints

- Primary endpoints: baPWV, echocardiographic parameters, CAC scores
- Secondary endpoints: blood cardiovascular biomarkers, mortality, PROs

CARTOON 연구 결과, cardiovascular benefit에서 online-HDF에 대한 HDx의 비열등성이 확인되었습니다.²³



- 심혈관 지표에 대한 분석 결과, 치료 기간 동안 HDx 및 online-HDF에서 baPWV, LVEF, LVMI, E/e' 변화에 차이가 없었습니다.²³
- Troponins I, troponins T, BNP, NT-proBNP, hsCRP, IL-6와 같은 심혈관 바이오마커의 변화는 두 치료군에서 유사하였습니다.²³

Several cardiovascular parameters were compared between patients undergoing HDx and online-HDF from the dialysis units of four tertiary referral hospitals in South Korea. 80 patients undergoing thrice-weekly hemodialysis were randomly assigned to receive either HDx with a Theranova membrane (n=43) or online-HDF (n=37). A linear mixed model and log-rank test were used to estimate the group differences. 65 patients had completed the trial.

baPWV=brachial-ankle pulse wave velocity; BNP=brain natriuretic peptide; CAC=coronary artery calcium; E=peak early mitral inflow velocity; e'=peak early diastolic mitral annular velocity; HDF=hemodiafiltration; HDx=expanded hemodialysis; hsCRP=high-sensitivity C-reactive protein; IL-6=interleukin-6; LVEF=left ventricular ejection fraction; LVMI=left ventricular mass index; NT-proBNP=N-terminal prohormone of brain natriuretic peptide; PRO=patient-reported outcome



Cardiovascular Outcomes



Online-HDF의 사용이 어려운 클리닉의 경우, 기존의 HD 치료 환자에서 HDx는 QoL 및 cardiovascular outcome 개선을 위한 치료적 대안이 될 수 있습니다.²³

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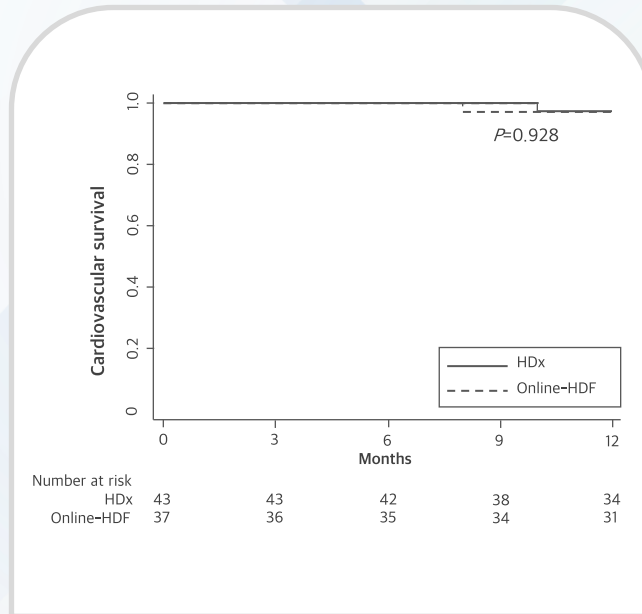
- Multicenter, prospective, open-label, randomized trial
- To compare cardiovascular parameters (HDx vs. online-HDF)
- N=80 (43 HDx, 37 online-HDF)
- 1 year study period

✔ Study endpoints

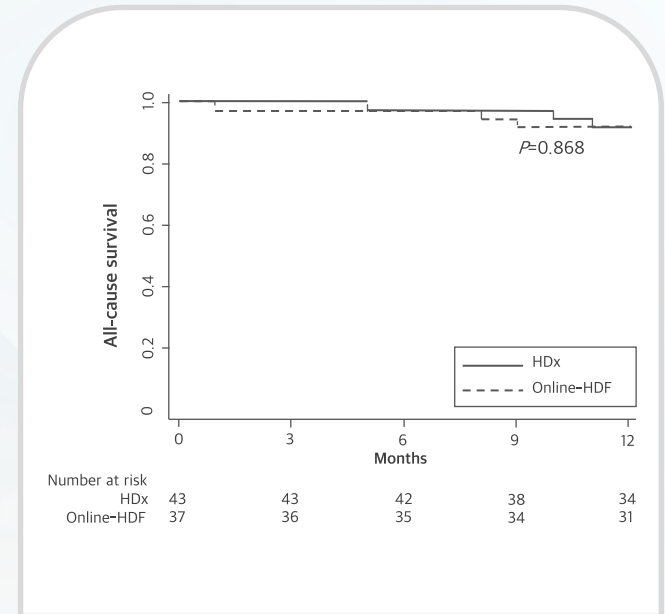
- Primary endpoints: baPWV, echocardiographic parameters, CAC scores
- Secondary endpoints: blood cardiovascular biomarkers, mortality, PROs

심혈관 관련 사망률 및 총 사망률에 대한 생존 곡선은 두 그룹 간에 차이가 없었습니다.²³

Kaplan-Meier curves of cardiovascular survival²³



Kaplan-Meier curves of all-cause survival²³



Several cardiovascular parameters were compared between patients undergoing HDx and online-HDF from the dialysis units of four tertiary referral hospitals in South Korea. 80 patients undergoing thrice-weekly hemodialysis were randomly assigned to receive either HDx with a Theranova membrane (n=43) or online-HDF (n=37). A linear mixed model and log-rank test were used to estimate the group differences. 65 patients had completed the trial.

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Patient-reported outcome 결과, 두 치료군 사이 DSI의 증상 중증도, 피로 정도, 투석 후 회복 시간은 유사하였습니다.²³

Linear mixed-effects model for the change in patient-reported outcomes²³

| Variables | Baseline values | Change from the baseline (mean and 95% CI) | | | |
|--|-----------------|--|---------|--------------------|---------|
| | | 6 months | P value | 12 months | P value |
| Number of symptoms in DSI | | | | | |
| HDx | 12 (5-20) | -2.0 (-3.8 to -0.3) | 0.024 | -1.4 (-3.3 to 0.5) | 0.140 |
| Online-HDF | 11 (4-16) | -0.5 (-2.3 to 1.4) | 0.634 | -1.0 (-2.9 to 1.0) | 0.321 |
| Between-group difference | | -1.6 (-4.2 to 1.0) | 0.231 | -0.4 (-3.1 to 2.3) | 0.765 |
| Overall symptom severity score in DSI | | | | | |
| HDx | 17 (10-37) | -2.1 (-6.1 to 1.9) | 0.299 | -2.7 (-6.8 to 1.5) | 0.208 |
| Online-HDF | 18 (6-27) | -1.4 (-5.6 to 2.8) | 0.517 | -1.3 (-5.7 to 3.1) | 0.567 |
| Between-group difference | | -0.7 (-6.5 to 5.1) | 0.814 | -1.4 (-7.4 to 4.6) | 0.651 |
| Degree of fatigue after dialysis | | | | | |
| HDx | 6 (5-7) | 0.1 (-0.6 to 0.9) | 0.702 | -0.6 (-1.3 to 0.2) | 0.164 |
| Online-HDF | 5 (3-6) | -0.3 (-1.1 to 0.5) | 0.513 | 0.1 (-0.8 to 0.9) | 0.880 |
| Between-group difference | | 0.4 (-0.7 to 1.5) | 0.459 | -0.6 (-1.8 to 0.5) | 0.287 |
| Recovery time after dialysis | | | | | |
| HDx | 3 (2-3) | 0 (-0.3 to 0.3) | 0.975 | 0 (-0.3 to 0.4) | 0.786 |
| Online-HDF | 2 (1-3) | -0.1 (-0.4 to 0.3) | 0.730 | -0.1 (-0.4 to 0.3) | 0.713 |
| Between-group difference | | 0 (-0.4 to 0.5) | 0.912 | 0.1 (-0.4 to 0.6) | 0.644 |

CI=confidence interval; DSI=dialysis symptom; HDF=hemodiafiltration; HDx=expanded hemodialysis; QoL=quality of life

Several cardiovascular parameters were compared between patients undergoing HDx and online-HDF from the dialysis units of four tertiary referral hospitals in South Korea. 80 patients undergoing thrice-weekly hemodialysis were randomly assigned to receive either HDx with a Theranova membrane (n=43) or online-HDF (n=37). A linear mixed model and log-rank test were used to estimate the group differences. 65 patients had completed the trial.

baPWV=brachial-ankle pulse wave velocity; CAC=coronary artery calcium; CI=confidence interval; DSI=dialysis symptom; HDF=hemodiafiltration; HDx=expanded hemodialysis; PRO=patient-reported outcome; QoL=quality of life



Cardiovascular Outcomes



Theranova를 통한 확장된 혈액투석 (HDx)으로, 혈장 내 Endothelial microvesicles (EMV)의 감소 및 투석 후 회복 시간의 개선을 보였습니다.¹⁸

> Study 6

A randomised study investigating the effect of medium cut-off haemodialysis on markers of vascular health compared with on-line haemodiafiltration (MoDal Study).

Kharbanda K, et al. Poster clinicaltrials.gov (NCT03510520).

Study design²⁴

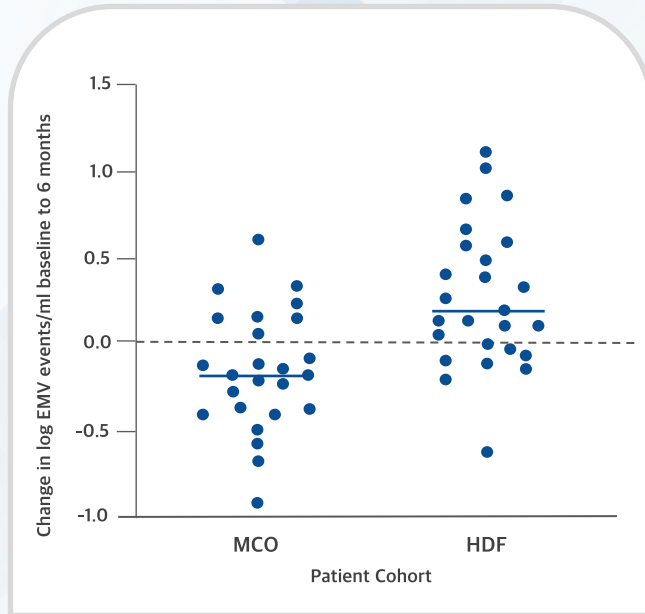
- Single-centre, pilot, open-label, randomised controlled study
- To investigating effect of MCO HD on markers of vascular health (vs. on-line HDF)
- N=63 (1:1 randomisation)
- 6 months study period

Study endpoints²⁴

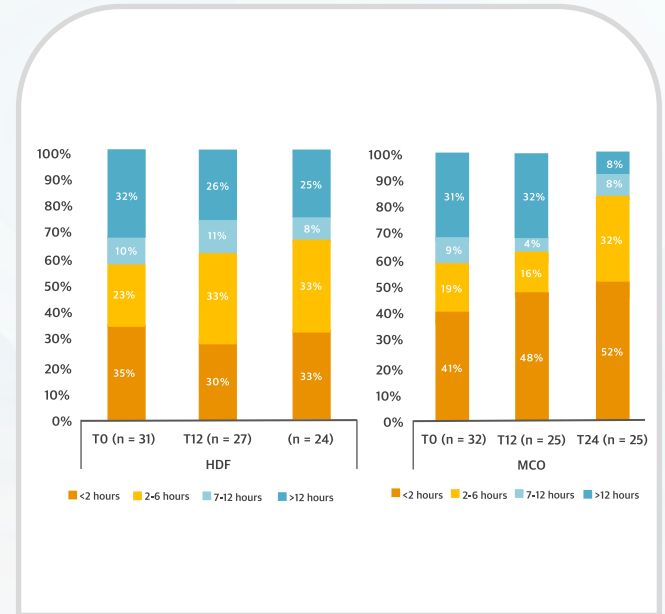
- Primary endpoints: effects of HDx treatment on EMV compared with HDF therapy
- Secondary endpoints: inflammatory cytokines, a panel of larger middle molecules, body composition monitoring, PROs

- MoDal 연구 결과, 치료 6개월 차 HDx 치료군의 경우 베이스라인 대비 EMV가 감소하였습니다 (p<0.05).¹⁸
- 투석 후 회복 시간이 < 6시간인 환자 비율이 HDx 치료군에서 더 높았습니다 (86% MCO vs 66% HDF, p=0.0524).¹⁸

Change in log EMV events/mL at 6 months compared to baseline¹⁸



Change in self-reported dialysis recovery time over 24 weeks¹⁸



Patients were randomised to 6 months MCO therapy or continue on existing HDF therapy. Pre-dialysis EMV was measured at baseline, 3 months and 6 months. 63 participants were randomised to either MCO or HDF and 50 participants (25 each group) completed the full protocol.²⁴

EMV=endothelial microvesicles; HD=hemodialysis; HDF=hemodiafiltration; HDx=expanded hemodialysis; MCO=medium cut-off; PRO=patient-reported outcome

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