Comparison of Ultrafiltration and Intravenous Diuretic Therapies in Patients Hospitalized for Acute Decompensated Biventricular Heart Failure

Akut Dekompanse Biventriküler Kalp Yetersizliği ile Yatırılan Hastalarda Ultrafiltrasyon ve İntravenöz Diüretiklerin Karşılaştırılması

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ABSTRACT

OBJECTIVE: Studies comparing ultrafiltration and diuretics in management of ADHF have shown controversial results. In this study, we compared the efficacy and safety of intravenous diuretic therapy and ultrafiltration in patients admitted with acute decompensated heart failure (ADHF) who had right ventricular dysfunction superimposed on left ventricular systolic dysfunction.

MATERIAL and METHODS: A total of 30 patients of whom 10 were in the ultrafiltration group and 20 were in the diuretic group were enrolled in this study and followed for 3 months.

RESULTS: At discharge, there were no significant differences between the ultrafiltration and diuretic groups in terms of weight loss , total fluid loss, and changes in serum creatinine. The clinical decongestion rates were similar in the two groups. Moreover, echocardiographic and biochemical parameters and alterations in renin and aldosterone levels, as measured to assess neurohormonal activation, had overlapping results between the two groups. When unwanted events were analyzed, transition to hemodialysis was seen in 20% of the patients in the ultrafiltration group and 5% of the patients in the diuretic group. The frequency of cardiac arrest and death were 40% in the ultrafiltration group and 10% in the diuretic group. Weight change, creatinine, and electrolyte levels of the patients at 1 and 3 months were also similar.

CONCLUSION: Despite the high frequency of hemodialysis transition, cardiac arrest, and death in the ultrafiltration group, safety of ultrafiltration could not be assessed because of inability to perform statistical analyses. Further studies are needed to investigate the practical uses of ultrafiltration in routine clinical practice.

KEY WORDS: Heart failure, Ultrafiltration, Diuretic therapy

ÖZ

AMAÇ: Akut dekompanse kalp yetersizliği (ADKY) tedavisinde ultrafiltrasyon ve diüretikleri karşılaştıran çalışmalarda çelişkili sonuçlar elde edilmiştir. Çalışmamızda ADKY nedeniyle yatırılan, sol ventrikül sistolik disfonksiyonu üzerine sağ ventrikül fonksiyon bozukluğunun süperpoze olduğu (biventriküler kalp yetmezliği) hasta grubunda intravenöz diüretik tedavisi ile ultrafiltrasyonu, etkinlik ve güvenilirlik açısından karşılaştırdık.

GEREÇ ve YÖNTEMLER: Çalışmamıza ultrafiltrasyon grubuna 10, diüretik grubuna 20 olmak üzere toplam 30 hasta alındı ve hastalar 3 ay takip edildi.

BULGULAR: Taburcu olurken; ultrafiltrasyon ve diüretik grupları arasında kilo kaybı, toplam sıvı kaybı ve serum kreatinin düzeyindeki değişiklik açısından istatistiksel olarak anlamlı bir fark bulunmadı. Klinik olarak sağlanan dekonjesyon oranı, her iki grupta benzerdi. Ekokardiyografik parametrelerdeki, diğer biyokimyasal parametrelerdeki değişim, nörohormonal aktivasyonu değerlendirmek için bakılan serum renin ve aldosteron düzeylerindeki değişim de gruplar arasında farklı bulunmadı. İstenmeyen olaylar değerlendirildiğinde; hemodiyalize geçme ultrafiltrasyon grubunda %20, diüretik grubunda %5 oranında, kardiyak arrest ve ölüm ise ultrafiltrasyon grubunda %40, diüretik grubunda %10 oranında görüldü. Hastaların 1 ay ve 3 ay sonraki kilo değişimi, kreatinin ve elektrolit düzeyleri de benzer bulundu.

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SONUÇ: Sağ ve sol kalp yetersizliğinin birlikte olduğu hastalara uygulanan ultrafiltrasyon ve diüretik tedavilerinin, kilo kaybı, toplam sıvı kaybı, klinik olarak dekonjesyonun sağlanması, böbrek ve kardiyak fonksiyonlarında değişim, renin ve aldosteron düzeylerindeki değişim yönünden birbirine üstünlüğü gösterilemedi. Hemodiyalize geçme, kardiyak arrest ve ölümün ultrafiltrasyon grubunda daha fazla saptanmasına rağmen, istatistiksel değerlendirme yapılamadığından, ultrafiltrasyonun güvenilirliği değerlendirilememiştir. Ultrafiltrasyonun tedavide rutin uygulamaya girmesi için daha kapsamlı çalışmalara ihtiyaç vardır.

ANAHTAR SÖZCÜKLER: Kalp yetersizliği, Ultrafiltrasyon, Diüretik tedavi

INTRODUCTION

The major cause of hospital admission in heart failure (HF) patients is dyspnea due to pulmonary congestion and fluid retention (1). Hypervolemia causes progression of HF and increases mortality in this group. Therefore, management of congestion is the single most important treatment approach in this patient group. Loop diuretics have long been used for this purpose. However, as the HF worsens, response to diuretics worsens and obtaining euvolemia becomes more difficult. In addition, diuretics have been associated with high morbidity and mortality due to their effects in increasing neurohormonal activation causing electrolyte imbalances and cardiac and renal dysfunction (2). Therefore, ultrafiltration has emerged as an alternative treatment to diuretic therapy. During the last decade, several randomized controlled trials were conducted to compare diuretics and ultrafiltration in acute decompensated heart failure (ADHF). The first study, RAPID-CHF (The Relief for Acutely Fluid Overloaded Patients with Decompensated Congestive Heart Failure) was published in 2005 (3). In this study, 20 patients had 8-hour ultrafiltration and 20 patients had diuretic treatment. After 24 and 48 hours, the ultrafiltration group had significantly better outcomes in hypervolemia symptoms and fluid loss, but there were no differences between the groups in terms of weight loss and the duration of hospital stay (3). UNLOAD (Ultrafiltration versus Intravenous Diuretics for patients Hospitalized for Acute Decompensated Heart Failure), the most sophisticated study on this subject, is a multi-center study that compared 200 patients in the diuretic and ultrafiltration arms (4). In this study, the weight and fluid loss at 48 hours were significantly better in the ultrafiltration group, but the dyspnea scores were moderately similar. The number of re-hospitalized patients was lower in the ultrafiltration group when compared to the diuretic group at 90 days follow-up. Ultrafiltration was shown to be a safe and effective method in ADHF treatment and suggested as an alternative to diuretic therapy (4). However, these results were not consolidated with upcoming studies. The CARRESS-HF (Cardiorenal Rescue Study in Acute Decompensated Heart Failure) study, which was conducted in 2012 and enrolled patients with cardiorenal syndrome, demonstrated that diuretic therapy was superior to ultrafiltration therapy at 96 hours (5). In a single-center study by Patarroyo, et al., 63 ADHF patients with diuretic resistance and renal failure underwent ultrafiltration and afterwards 37 patients (59%) were required to undergo hemodialysis during their hospital course and 9 patients (14.3%) became dialysis-dependent after discharge (6).

Our current data obtained from the literature has been limited to clarify the efficacy and safety of ultrafiltration in management of ADHF. The study populations had great heterogeneities and the results obtained were therefore controversial. In addition, the optimal treatment of ultrafiltration (duration, velocity, and termination criteria) has not been fully established. The number of studies comparing these two treatment modalities in terms of cardiac functions and neurohormone levels is also limited. Further studies are needed to include ultrafiltration in routine clinical practice. In this study, we aimed to investigate the effects of ultrafiltration and diuretic therapies on cardiac and renal functions, as well as neurohormonal levels in patients with concomitant right and left ventricular failure.

MATERIALS and METHODS

The present study is a randomized prospective controlled study that compares ultrafiltration and diuretic therapies in patients who were admitted to our hospital's departments of cardiology and nephrology. Patients hospitalized for heart failure were randomly assigned in a 1:1 ratio to either ultrafiltration therapy or diuretic therapy. The study was approved by the local ethics committee and informed consent was obtained from individual patients.

Patient Selection: Patients who were admitted with HF, over 18 years old, had hypervolemia as detected by at least 2 findings listed below, and had objective criteria of right ventricular failure as determined by echocardiography (TAPSE <16 mm, S velocity <10 mm/sn, moderate to severe dilation of right ventricle and moderate to severe dilation of right atrium) were enrolled in this study.

1- Peripheral edema ≥2 +

2- Central venous pressure >20 cmH_2O

3- Pulmonary edema or pleural effusion detected by radiography

4- Hepatomegaly or ascites

5- Crackles on auscultation of lung, paroxysmal nocturnal dypsnea, or orthopnea

Exclusion criteria:

1- Acute coronary syndrome
2- Serum creatinine >3,5 mg/dl
3- Systolic blood pressure ≤ 90 mmHg
4- Hemodynamic instability requiring inotropic drug use
5- Patients with comorbidities that required long-term hospitalization
6- Conditions in which anticoagulation was contraindicated
7- Systemic infection
8- Heart transplantation

Study Protocol: All oral diuretic agents were stopped but the patients continued to take their angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), beta blockers, and digoxin. Patients were divided into two groups, namely ultrafiltration and diuretic groups, 8 hours after admission and followed for 90 days.

Ultrafiltration group:

- The maximal rate of ultrafiltration was 500 cc/hour.
- Duration and rate of ultrafiltration were determined by clinician.
- Intravenous and oral diuretics were withheld during ultrafiltration.
- The rate of blood flow was set to 50-100 ml/min.
- A central venous catheter was used.
- Standard heparin was given.

Diuretic group:

- Intravenous diuretic treatment was administered with an intravenous bolus or continuous infusion.
- Diuretic therapy was provided with the maximal tolerable dose of furosemide.

Assessment and Follow-up

The weight of the patients was measured at hospital admission, daily during the hospital stay, and at 30 and 90 days after discharge. Vital signs, complete blood count, biochemical tests, and physical examination were recorded daily during the hospital stay and days 30 and 90 after discharge. The B-type natriuretic peptide (BNP) level was measured at the beginning of the study and at discharge. Echocardiography was performed at admission and prior to discharge in the diuretic group, and before and after ultrafiltration in the ultrafiltration arm. Plasma renin activity and aldosterone level were measured with radioimmunoassay in blood samples obtained after 2 hours of bed rest at admission and discharge. New York Heart Association (NYHA) functional capacity was evaluated at admission and discharge. During the 90 days of follow-up, the number of hospital re-visits and re-admissions due to ADHF were recorded.

Statistical Analysis

All statistical analyses were performed with the SPSS package program (version 14.0). Non-parametric variables were analyzed with the Mann-Whitney U test and p values lower than 0.05 were accepted to be statistically significant. The significance of the differences between the groups was tested using Fisher's exact test.

RESULTS

A total of 30 patients were enrolled in this study of whom 10 were in the ultrafiltration group and 20 were in the diuretic group. Another nine patients had been enrolled to the ultrafiltration group but these 9 patients were excluded from the study as ultrafiltration therapy had been terminated because of technical reasons such as ineffective operation of the ultrafiltration device and clotting in the set. Demographic, clinical and hemodynamic features of the patients are summarized in Table I. There were no significant differences in baseline characteristics between the two study groups ($p > 0.05$).

The blood flow rate was 50-100 mL/hour and the ultrafiltration rate was 150-400 mL/hour in the ultrafiltration group. Mean ultrafiltration duration was 20.5 ± 4.6 hours.

Average daily furosemide dose in the diuretic group was 164.1 ± 51.3 mg. Termination criteria for ultrafiltration and diuretic therapy was set for achievement of satisfactory clinical decongestion.

The comparison of the two groups for weight loss and creatinine levels is shown in Figures 1 and 2. Weight loss as compared to baseline values was significantly higher in the ultrafiltration group when compared to the diuretic group at days 1 and 2 ($p = 0.001$). However, there were no significant differences between the groups at the other days, including discharge, and 1 and 3 months later.

There were no significant differences between the groups in terms of changes in creatinine levels. During hospitalization, changes in creatinine levels from baseline in each group were not statistically significant (Figure 2).

The duration of hospital stay was 7.15 ± 2.3 days in the diuretic group and 6.6 ± 1.0 days in the ultrafiltration group, but no significant difference was observed between the groups ($p = 0.581$).

Total net fluid loss was calculated as the difference between daily fluid intake and urine excretion in the diuretic group, and daily fluid intake and the amount of ultrafiltrate in the ultrafiltration group. Net fluid loss was 7.87 ± 1.83 ml in ultrafiltration group and 6.88 ± 4.21 ml in the diuretic group. However, there was no significant difference between the two groups for total net fluid loss ($p = 0.052$) (Table II).

Table I: Baseline characteristics of patients prior to treatment.

	Ultrafiltration group (n=10)	Diuretic group (n=20)	P value
Age (years) Range	66.5 ± 9.8 52-79	66.8 ± 10.2 47-81	0.930
Males (%)	60	65	0.789
History of hypertension (%)	100	85	0.197
CABG (coronary artery by-pass graft) history (%)	60	45	0.180
History of myocardial infarction (%)	30	55	0.196
History of COPD (%)	40	35	0.789
Diabetes Mellitus (%)	60	50	0.605
Ejection fraction (%) Range	32.1 ± 11.3 15-48	31.7 ± 7.2 20-45	0.929
NYHA functional class Range	3.0 ± 0.81 2-4	2.95 ± 0.75 2-4	0.869
Weight (kg) Range	73.8 ± 13.3 53-91	86.5 ± 20.9 55-130	0.094
Systolic blood pressure (mmHg) Range	118 ± 12.2 100-140	112 ± 16.7 80-130	0.448
Pulse/min Range	80 ± 11.2 68-100	78.4 ± 12.3 65-120	0.595
Blood urea nitrogen (mg/dl) Range	48.6 ± 25.8 13-93	37.1 ± 15.1 12-68	0.271
Creatinine (mg/dl) Range	1.56 ± 0.8 0.6-3.2	1.39 ± 0.5 0.8-2.7	0.482

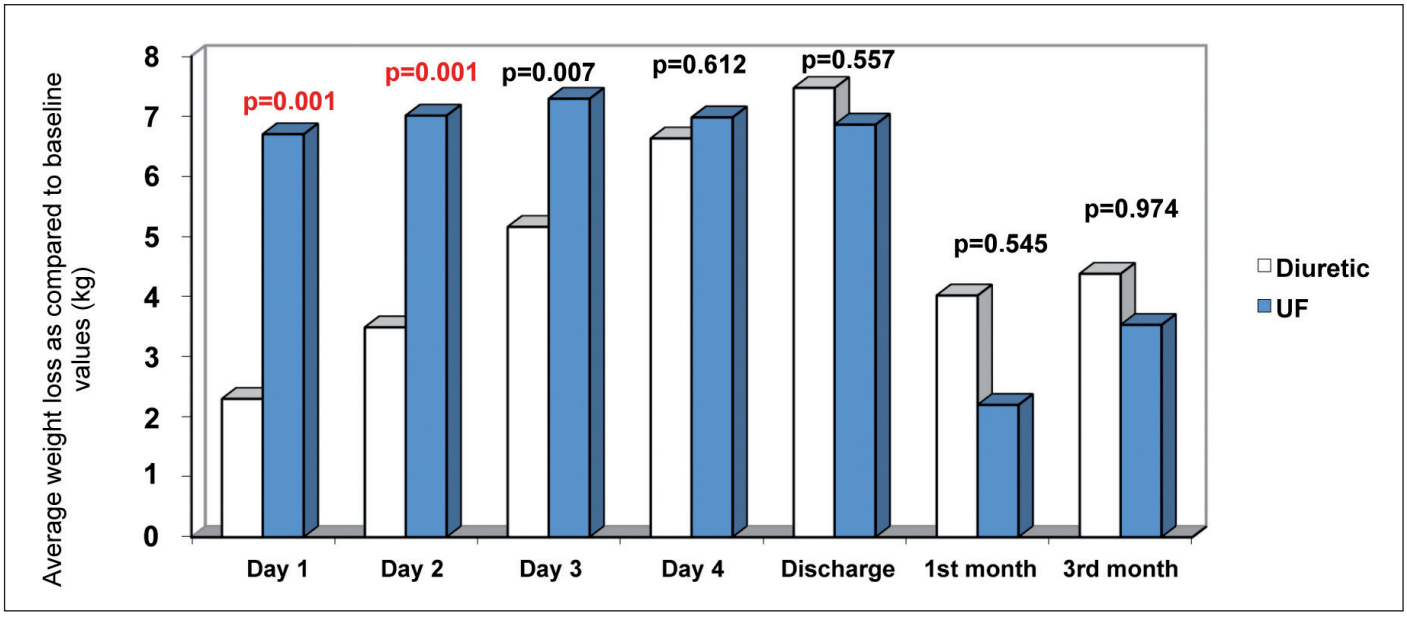

Figure 1: *Day-by-day comparison of diuretic and ultrafiltration groups for weight loss.*
Weight loss as compared to baseline values was significantly higher in the ultrafiltration group when compared to the diuretic group at days 1 and 2 (p = 0.001). However, there were no significant differences between the groups at the other days, including discharge, and 1 and 3 months later.

Decongestion was described as having no pretibial edema, dyspnea, orthopnea, or crackles on auscultation during the entire hospital stay. Clinical decongestion was obtained in 7 out of 10 patients (70%) in the ultrafiltration group, and 16 out of 20 patients (80%) in the diuretic group. There were no statistically significant differences between the two groups (Table II).

Serum renin and aldosterone levels were measured at admission and discharge to assess neurohormonal activation in the two groups. There were no statistically significant differences between the two groups at admission or discharge. Moreover, there were no significant differences between the two groups in terms of changes in baseline levels at discharge.

In order to evaluate the effect of treatment on cardiac functions, echocardiography was performed at admission and discharge in the diuretic group, and before and after ultrafiltration in the ultrafiltration group. There were no significant differences

Table II: Comparison of ultrafiltration and diuretic groups for net fluid loss, clinical decongestion, and alterations in biochemical and echocardiographic parameters during the entire hospital stay.

Parameter	Ultrafiltration (n=10)	Diuretic (n=20)	P value
Change in serum sodium level at day 4 as compared to baseline sodium (mmol/L)	-0.5 ± 5.2	0.65 ± 5.7	0.691
Change in serum potassium level at day 4 as compared to baseline potassium (mmol/L)	0.08 ± 0.9	0.36 ± 0.7	0.537
Change in serum NT-proBNP level at day 4 as compared to discharge level (ng/L)	-5567 ± 3855	-4393 ± 5155	0.218
Clinical decongestion achieved at discharge, n/total n (%)	7/10 (70)	16/20 (80)	0.680
Total net fluid loss at discharge (mL)	7872 ± 1829	6882 ± 4211	0.052
Change in echocardiographic parameters at discharge as compared to baseline levels Ejection fraction (%)	1.0 ± 3.2	0.25 ± 1.1	0.576
TAPSE (cm)	-0.03 ± 0.1	-0.04 ± 0.1	0.872
Pulmonary artery pressure (mm/Hg)	-2.1 ± 4.6	-0.35 ± 7.1	0.835
Left atrial diameter (cm)	-0.21 ± 0.3	-0.29 ± 0.2	0.400

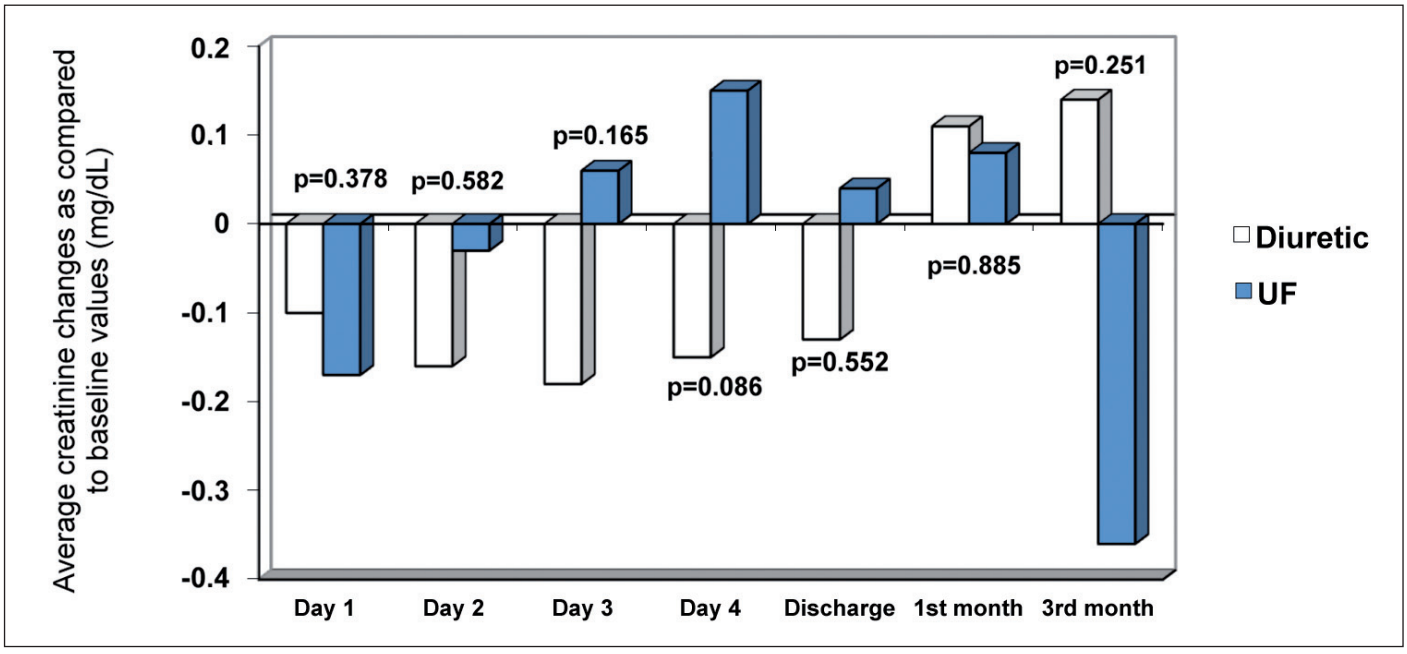

Figure 2: *Day-by-day comparison of the diuretic and ultrafiltration groups for creatinine changes.*
There were no significant differences between the groups in terms of changes in creatinine levels. Creatinine levels decreased in the diuretic group at days 3, 4, and at discharge, but increased in the ultrafiltration group. However, these changes were not statistically significant.

between the two groups for ejection fraction, left atrial diameter, pulmonary artery pressure, and TAPSE measurements before and after treatment. Moreover, there were no statistically significant changes in echocardiographic findings compared to baseline measures in the two groups (Table II).

Biochemical and echocardiographic changes in the groups are summarized in TableII. There were no significant differences between the two groups in terms of sodium and potassium changes at day 4 (Table II). There was a substantial reduction in NT-proBNP levels in both groups at discharge but there was no statistically significant difference in its levels between the two groups ($p = 0.218$).

The number of re-admissions to hospital with an ADHF attack in 3 months was 1.0 ± 0.8 in the ultrafiltration group and 1.4 ± 1.2 in the diuretic group. There was no significant difference between the two groups for rates of hospital re-admission ($p=0.534$).

When unwanted events were evaluated, 1 patient (10%) had hematoma development at the catheter insertion site. Infection and bleeding complications were not seen in either group. In the ultrafiltration group, two patients (20%) were switched to hemodialysis during follow-up. Hypotension was seen in 1 patient (10%) in the ultrafiltration group, and 2 patients (10%) in the diuretic group. Cardiac arrest and death were seen in 4 patients (40%) in the ultrafiltration group and 2 patients (10%) in the diuretic group. However, statistical analysis for unwanted events could not be performed due to the low number of cases.

DISCUSSION

In this study, we compared the efficacy and safety of ultrafiltration and diuretic therapies in patients admitted with ADHF who had biventricular heart failure. There were no significant differences between the two treatment groups in terms of weight loss and net fluid loss. There were also no differences between two groups for echocardiographic parameters; changes in serum creatinine, electrolytes, renin, aldosterone levels; and the number of re-hospitalizations in three months.

Prior randomized controlled trials evaluated treatment efficacy 48 and 36 hours after therapy and this duration is very short for diuretic treatment (3, 4). Moreover, ultrafiltration procedure is performed during the first 48 hours, and thus higher net fluid and weight loss is expected in 48 hours. Diuretic treatment continues during the entire hospital stay and therefore, assessment of total fluid loss when the treatment ends would be more accurate when comparing the two groups. In this study, we compared net fluid loss in the two groups during the entire hospital stay, and there was no statistically significant difference between the two groups in terms of total net fluid loss ($p = 0.052$) (Table II). During the first 48 hours, the ultrafiltration group had significantly higher weight loss ($p = 0.001$) but there were no significant weight loss differences between the two groups during follow-up, at discharge, and 1 month after discharge (Figure 2). Similar to our study, fluid and weight loss at 96 hours were not significantly different between the two groups in the CARESS-HF study (5).

There were no significant differences between the two groups for congestion signs, including dyspnea, pretibial edema, and crackles (Table II). Similarly in the UNLOAD study, the ultrafiltration group failed to demonstrate a superiority in terms of quality of life improvement and regression of dyspnea despite higher degrees of weight and fluid loss at 48 hours (4). Other studies also showed similar results between the two groups in terms of improvement in heart failure symptoms (3, 5).

In our study, 9 patients in the ultrafiltration group could not complete the treatment for technical reasons and were excluded from the study. While the proportion of patients withdrawn from the study in CARRESS-HF was 18%, we had a higher rate of 45 % in our study. The reason may be that our patients could not adapt to long-term ultrafiltration treatment. Termination of treatment is mostly caused by stopping ultrafiltration devices and clotting in the set due to frequent mobilization of patients.

An important limitation of the UNLOAD study is the lower diuretic dose, which was 75-80% of maximal dose. In the study, the diuretic group received an average dose of 180 mg/day furosemide. However, the average furosemide dose was 164±50 mg in our study. Our doses were also suboptimal when compared to recommended maximal dose. However, since most of our patients had clinical decongestion at their given doses, we did not need to escalate the dose. In the CARRESS-HF study, stepwise diuretic treatment was performed with 3-5 L/day of diuresis and the treatment was supported with metolazone, thiazides, and vasoactive drugs to overcome diuretic resistance (5). Therefore, pharmacologic treatment was better designed in the CARRESS-HF study. Ultrafiltration was also continued for 40 hours and 200 mL fluid was removed every hour. In the CARRESS-HF study, the duration of ultrafiltration was longer, and its rate was slower. Despite these differences, increase in the serum creatinine was significantly higher in the ultrafiltration group when compared to the diuretic group at 96 hours after randomization ($p = 0.003$) (5). In our study, the rate of ultrafiltration was 150-400 mL/hour and the average duration was 20.5 hours. In the CARESS-HF study, 96 hour creatinine levels were higher in the ultrafiltration group, but there were no differences between groups at day 7 and month 1. This means the ultrafiltration group had a transient impairment in renal function. Interestingly, transient increases in creatinine levels in patients with ADHF might not indicate a poor prognosis (7). In a study published in 2011, renal dysfunction occurring during treatment in ADHF patients was attributed mostly to underlying primary or secondary renal disease (DM, glomerulonephritis, etc) rather than the effect of treatment itself (8). Increased azotemia is seen primarily in patients with pre-existing renal dysfunction. In addition, a single creatinine measurement might not reflect

the underlying renal dysfunction. In a study by Rogers et al., the effect of ultrafiltration and diuretic treatments on glomerular filtration rate (GFR) and renal plasma flow was investigated. Forty-eight hours after the treatment, there were no significant differences in GFR and renal plasma flow between two groups despite a decrease in GFR in both groups (9). In a recent study by Hanna et al., cystatin C was used to evaluate renal function, and there were no significant differences in cystatin C levels 48 hours after the treatment (10). In these studies, follow-up was limited to 48 hours and parameters other than creatinine were used to evaluate renal functions. Their data revealed that both treatments had similar effects on kidney functions.

Despite no significant differences in creatinine levels in our study, 20% of the patients in the ultrafiltration group and 5% of patients in the diuretic group were transitioned to hemodialysis. In a single center study by Patarroyo, et al., there were no significant differences in creatinine levels before and after ultrafiltration. After ultrafiltration treatment, 37 patients (59%) were transitioned to hemodialysis and 9 patients (14.3%) were dependent on dialysis after discharge (6). Patients with advanced heart failure who were resistant to diuretics and had renal function disorders were enrolled in this study. Similarly, our study enrolled more severe cases with biventricular failure. These results support the idea that ultrafiltration might have an adverse effect on kidney functions among patients with advanced heart failure.

Our patient cohort was different from that of previous studies in that we enrolled patients with right heart failure superimposed on left heart failure. We also evaluated echocardiographic changes and cardiac functions in our study cohort, before and after treatment. To the best of our knowledge, these have not been included in prior studies. There were no significant changes in echocardiographic parameters including EF, left atrial diameter, TAPSE, and pulmonary artery pressure before and after treatment. There was also no difference between the two groups in terms of alterations in these parameters (Table II). Previously in a 1993 study, echocardiography was performed and demonstrated that right and left filling pressures were lower in patients who underwent ultrafiltration (11). We did not assess filling pressures, but a positive effect of diuretic therapy or ultrafiltration could not be shown in other parameters showing right and left heart failure. This might be attributed to the our patient cohort, which was composed of more severe patients with biventricular heart failure. In a study by Patarroyo et al., ultrafiltration was performed in diuretic-resistant patients and meaningful improvements were obtained in pulmonary artery pressure, central venous pressure, mean pulmonary wedge pressure, and cardiac index (6).

We measured renin and aldosterone levels in two groups in order to assess the presence of neurohormonal activation. None of the groups had significant increases in aldosterone levels. Similarly, changes in renin and aldosterone levels at admission and discharge in the two groups were similar. Prior studies reported that ultrafiltration enabled more effective sodium elimination when compared to diuretics with a lower degree of neurohormonal activation (12-14). In another study by Marenzi et al., patients who underwent ultrafiltration had lower levels of plasma norepinephrine, renin, and aldosterone (15). In our study, renin and aldosterone levels were measured at discharge rather than the first 48 hours during when fluid loss was maximum, which might explain the lower level of neurohormonal activation.

Early-term mortality (3 months) was 40% in the ultrafiltration group and 10% in the diuretic group. Despite the higher frequency of mortality in the ultrafiltration group, statistical analysis could not be performed due to the lower number of patients. In our study, the frequency of diabetic patients was 60% in the ultrafiltration group and 50% in the diuretic group. Although the disparity was not statistically significant, the higher frequency of mortality in the ultrafiltration group might be caused by higher frequency of diabetic patients. Our patient cohort had concomitant right and left heart failure and thus we enrolled more severe patients as compared to other studies. However, the mortality rate in the diuretic group was similar to other studies (10%) while the mortality rate in the ultrafiltration group (40%) was significantly higher. These results suggest that ultrafiltration might be associated with an increase in mortality in patients with combined right and left heart failure.

The CUORE (Continuous Ultrafiltration for Congestive Heart Failure) study published in 2014 compared ultrafiltration and standard medical therapy with the longest duration of follow-up (16). Although the weight loss was similar in the two groups at discharge (7.5 ± 5.6 in ultrafiltration group and 7.9 ± 9.0 kg in control group), re-hospitalization due to heart failure during 1 year follow-up was less frequent in the ultrafiltration group ($p = 0.002$). Similarly, the UNLOAD study also showed lower frequency of re-hospitalization in the ultrafiltration group (4). In our study, re-hospitalization rates due to an ADHF attack during the 3-month follow-up was similar in the ultrafiltration and diuretic groups ($p = 0.534$).

In studies assessing the efficacy of ultrafiltration, re-hospitalization rates during follow-up were recorded, but treatment in these re-admissions were not recorded, except the CUORE study. In most of these studies, ultrafiltration was given for a single session, and the probability of diuretic use is higher in re-admissions. Most of the patients continue their oral diuretic treatment after discharge. Intermittent ultrafiltration after discharge (once a month or every other month) might be accepted as a treatment option. It is difficult to confirm that a single session of ultrafiltration might have an impact on short and long-term life expectancy (17). Future studies are needed to determine the efficacy and safety of giving the same treatment to ADHF patients who were treated with ultrafiltration or diuretic therapy and re-admitted.

In this study, the effects of ultrafiltration and diuretic treatments on fluid and weight loss, regression of congestion symptoms, neurohormone levels, and changes in echocardiographic parameters were similar. Although not statistically analyzed, death and transition to hemodialysis were more frequent in the ultrafiltration group. These results suggest that ultrafiltration might be associated with increased mortality in patients with biventricular failure and might adversely affect renal function.

One of the pitfalls in ultrafiltration treatment is lack of clarity in the optimal ultrafiltration rate, duration and criteria to terminate ultrafiltration. Current data failed to demonstrate a superiority of ultrafiltration on diuretics. Since ultrafiltration is an invasive procedure with complications including hypotension, catheter-related complications, and bleeding due to the use of systemic anticoagulation, current guidelines recommend its use in patients who did not respond to optimal doses of diuretics (18,19). In addition, suitable patients might be treated with both modalities. Intermittent application of ultrafiltration might be more advantageous in terms of lower doses of diuretic therapy, and a decrease in diuretic resistance.

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