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ORIGINAL RESEARCH - CLINICAL

Safety, Feasibility of Controllable Decrease of Vena Cava Pressure by Doraya Catheter in Heart Failure

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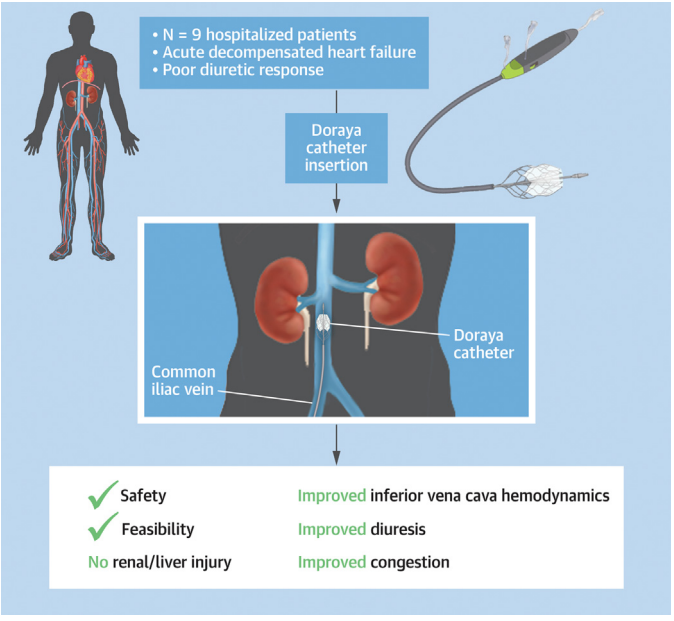
VISUAL ABSTRACT



Zymliński R, et al. J Am Coll Cardiol Basic Trans Science. 2023;8(4):394-402.

HIGHLIGHTS

- **Elevated renal venous pressures are related to decreased renal perfusion pressures, which translate to renal dysfunction and an increased risk of worsening renal function.**
- **The Doraya catheter was developed to perform a transient and controllable modification of renal venous pressure by creating a gradient in the inferior vena cava below the renal veins.**
- **In 9 acute heart failure patients, Doraya catheter deployment created a gradient in the inferior vena cava (below vs above the device), resulting in a decrease of central venous pressure above the catheter from 18.4 ± 3.8 mm Hg to 12.4 ± 4.7 mm Hg ($P < 0.001$).**
- **The procedure was found to be safe, with no adverse events related to increased venous pressures below the catheter or embolic events during or following the procedure.**

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A research letter containing a small portion of the FIH study results was published under the THT 2022 Shark Tank special issue of *JACC: Basic to Translational Science* in March 2022 (Zymliński R, Dierckx R, Biegus J, Vanderheyden M, Bartunek J, Ponikowski P. Novel IVC Doraya catheter provides congestion relief in patients with acute heart failure. *J Am Coll Cardiol Basic Trans Science*. 2022;7(3):326-327. https://doi.org/10.1016/j.jacbts.2022.02.013.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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SUMMARY

Lowering elevated central venous pressure may reduce renal dysfunction in acute heart failure (AHF) patients. The Doraya catheter lowers renal venous pressure by creating a gradient in the inferior vena cava below the renal veins. Here, we present a first-in-human feasibility study of the Doraya catheter performed on 9 AHF patients. We assessed the safety, feasibility, and acute clinical (hemodynamic and renal) effects of transient Doraya catheter deployment when added to the standard diuretic-based regimen in AHF patients with a poor diuretic response. The procedures decreased central venous pressure from 18.4 ± 3.8 mm Hg to 12.4 ± 4.7 mm Hg ($P < 0.001$) and improved mean diuresis and clinical signs of congestion. No device-related serious adverse events were observed. Thus, Doraya catheter deployment was safe and feasible in AHF patients. (First In Human Study of the Doraya Catheter for the Treatment of AHF Patients; NCT03234647)

ABBREVIATIONS AND ACRONYMS

AHF = acute heart failure
CVP = central venous pressure
eGFR = estimated glomerular filtration rate
HF = heart failure
IVC = inferior vena cava
PCWP = pulmonary capillary wedge pressure
SAE = serious adverse event
SBP = systolic blood pressure

Central venous pressure (CVP) plays a critical role in renal function during heart failure (HF).[1,2] Higher renal venous pressures are related to lower renal perfusion pressures (defined as the difference between the renal artery and vein pressures), which further translate to renal dysfunction, a decrease of estimated glomerular filtration rate (eGFR), and an increased risk of worsening renal function.[1,2] Indeed, initial experience indicates that correcting the elevated pressure may be beneficial in reducing renal dysfunction in acute heart failure (AHF).[3]

The Doraya catheter was developed to perform a transient and controllable modification of renal venous pressure by creating a gradient in the inferior vena cava (IVC) below the renal veins (**Figure 1**). The device is introduced percutaneously, and its deployment results in a temporary decrease of renal venous pressure at the cost of transitory obstruction of the venous outflow from the lower extremities. Here, we present early results of a first-in-human Doraya catheter use in 9 HF patients. The initial results have been presented in a research letter submitted to *JACC: Basic to Translational Science* simultaneously with the Technology and Heart Failure Therapeutics 2022 Shark Tank.[4] Here, we present the complete study design and results.

MATERIALS AND METHODS

We present the results of the DORAYA trial (First In Human Study of the Doraya Catheter for the Treatment of AHF Patients; NCT03234647), a nonrandomized, open-label, single-arm, prospective study that was conducted in 4 European institutions between January 2018 (inclusion of the first patient) and April 2021 (study completion). This is the first-in-human use of the Doraya catheter for a controlled, transient decrease of renal venous pressure in AHF patients with a poor diuretic response. The study protocol was approved by the local ethics committee, and studies were conducted in accordance with the Declaration of Helsinki. All patients signed informed consent before enrollment.

DORAYA CATHETER DESCRIPTION. The Doraya catheter is a novel IVC flow regulator catheter designed for transient use (<12 hours). The Doraya temporarily reduces CVP and renal afterload. The catheter is inserted into the IVC and deployed below both renal veins to assist in hemodynamic management of hospitalized AHF patients in conjunction with diuretic therapy. The catheter includes a flexible nitinol frame premounted on the distal end of the catheter. A hydrophilic polyurethane layer covers the adjustable distal portion of the frame to regulate blood flow with physician-controlled adjustments. The catheter provides access to IVC pressure measurements above and below the distal flow regulator.

The device is deployed via percutaneous vascular access under fluoroscopy using the radiopacity characteristics of the nitinol frame and radiopaque tip. The catheter is 12-F outer diameter, with a maximum frame diameter of 25 mm, compatible with standard 0.035-inch guidewires.

Removal is done under fluoroscopy guidance in a cath lab or bedside by remounting the outer shaft on the catheter frame and removing it from the body.

DORAYA CATHETER PLACEMENT. First, the size of the inferior vena cave was measured under standard fluoroscopy to ensure the device fits properly and deployment is feasible. The Doraya catheter was then placed percutaneously in the inferior vena cava below the renal veins under fluoroscopic control (**Figure 1**).

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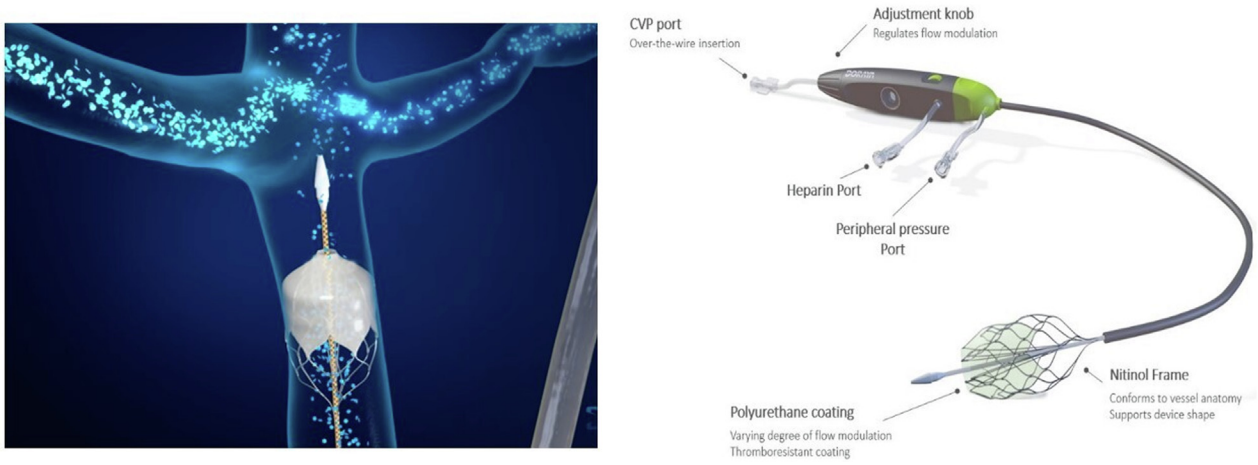
FIGURE 1 The Concept and Visualization of Doraya Catheter



CVP = central venous pressure.

Before the device was introduced, all patients received a bolus of unfractionated heparin with a subsequent infusion with target activated clotting time (≥250 seconds) and a single dose of dual antiplatelet therapy (300 mg of aspirin and 300 mg of clopidogrel). The activated clotting time was then monitored during the procedure at 1-hour intervals. The Doraya catheter was deployed for up to 12 hours. The termination of the Doraya catheter treatment and withdrawal of the catheter were left to the investigators' discretion.

STUDY DESIGN AND PATIENTS. The study was designed to investigate the safety, feasibility, and clinical (hemodynamic and renal) effects of the Doraya catheter when added to the standard diuretic-based regimen in patients with AHF with a poor diuretic response. Each patient served as its own control, as each patient underwent at least 24 hours of standard care and assessments before catheter deployment.

Patients were treated according to the current European Society of Cardiology guidelines. The diuretic dosage and management before the procedure were decided by the treating physician. During Doraya catheter deployment, the patient received at most the same diuretic dose and administration method as the previous day. In the morning, patients received the diuretic agents just after Doraya catheter deployment, and urine output was measured from that exact time point.

During the study, patients were closely monitored for adverse events, particularly for catheter thrombosis, catheter misplacement or migration, lower extremities edema, and other potential complications of elevated venous pressure below the device. Additionally, all patients had Swan-Ganz catheter hemodynamic monitoring during the procedure (see later in the text).

The complete list of all inclusion/exclusion criteria is provided in the Supplemental Appendix. Because the study was conducted to assess the safety and performance of the Doraya catheter in AHF patients, presenting persistent volume overload and poor response to diuretic treatment, the most relevant inclusion criteria for the study were:

1. The subject is hospitalized with a primary diagnosis of congestive AHF.
2. There is evidence of fluid overload (for details, see the Supplemental Appendix).
3. The subject responded insufficiently to standard diuretic therapy, meeting the following criteria:
   Received >80 mg of furosemide per day or an equivalent, or >1.5× the subject's chronic baseline diuretic level with at least 1 of the following:
   a) Weight reduction of <0.4 kg per 40 mg of furosemide (or equivalent) after 18 to 24 hours of diuretic agent initiation or;
   b) Urine output <0.75 mL/kg/h per 40 mg of furosemide (or equivalent) after 18 to 24 hours of diuretic agent initiation.
4. IVC with minimal inspiratory collapse is diagnosed by cardiac ultrasonography.

5. CVP >12 mm Hg was confirmed at the beginning or before the catheterization procedure.

The relevant exclusion criteria were:

1. Systolic blood pressure was <90 mm Hg at the time of screening.
2. Patient has severe renal dysfunction (eGFR <18 mL/min/1.73 m^2 body surface area), or the subject is on chronic dialysis.
3. The subject has a history of deep vein thrombosis and/or pulmonary embolism.

From baseline assessments and during the entire period of device deployment, close clinical evaluation and hemodynamic monitoring were performed with regular blood and urine sampling. Dyspnea was measured using a 7-point Likert scale, and edema by a pitting edema score. All patients were followed up for 60 days.

OUTCOMES. The study was conducted to determine the safety, feasibility, and tolerability of the Doraya system in patients with AHF. Thus, the device or procedure-related serious adverse event (SAE) rate through 30 days was the primary outcome. The events of interest included (but were not restricted to) bleeding, access site complications, vascular damage, catheter thrombosis, catheter misplacement or migration, worsening of lower extremities edema or other potential complications of elevated venous pressure below the device, air embolism, deep vein thrombosis, and other thrombotic events.

The primary feasibility endpoints were technical success, defined as the ability to position the catheter below the renal veins, regulate the flow in the IVC by creating a gradient pressure of at least 2 mm Hg, and withdraw the catheter safely.

Additional investigational efficacy endpoints included renal assessments with a particular interest in diuresis (measured during device deployment), serum creatinine, and natriuresis (only selected cases).

Clinical evaluation of congestion signs and symptoms was performed at baseline, at the end of device deployment, and after 48 hours. Reporting was based on physician assessment of edema (0 to 4 scale, with 0 indicating no edema) and patient reporting of dyspnea (Likert scale).

LABORATORY TESTS. The following laboratory measurements in peripheral blood and urine were assessed using standard methods in local laboratories:

1. Hematology: hemoglobin, hematocrit, leukocytes, platelets
2. Serum electrolytes: sodium, potassium
3. renal tests: creatinine; estimated glomerular filtration rate by MDRD (Modification of Diet in Renal Disease) method was calculated (eGFR)
4. Plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP)
5. Urine spot samples: electrolytes: sodium, potassium, creatinine, urea

HEMODYNAMIC MONITORING. All patients had a Swan-Ganz catheter inserted, and central

TABLE 1 Baseline Characteristics of Patients Treated With Doraya Catheter (N = 9)

Age, y	69 ± 9
Sex	
Male	7 (78)
Female	2 (22)
Systolic blood pressure, mm Hg	112 ± 23
Diastolic blood pressure, mm Hg	69 ± 11
Heart rate, beats/min	75 ± 15
Left ventricular ejection fraction, %	24 ± 12
Hemoglobin, g/dL	11.5 ± 2
Bilirubin, mg/dL	1.4 ± 0.5
eGFR, mL/min/1.73 m^2	31.1 ± 12.4
Creatinine, mg/dL	2.3 ± 0.7
NT-proBNP, pg/mL[a]	8,263 ± 8,520 (n = 7)
Baseline urine output, mL/h	77.1 ± 25
NYHA functional class	
II	2 (22)
III	3 (33)
IV	4 (44)
Medical history	
Hypertension	4 (44)
Ischemic heart disease	7 (78)
Atrial fibrillation	7 (78)
Cerebrovascular disease	2 (22)
Left ventricular hypertrophy	2 (22)
Diabetes	5 (56)
Chronic lung disease	1 (11)
Concomitant medications at baseline	
Loop diuretics	9 (100)
MRA	7 (78)
Other diuretic agents	7 (78)
Beta-blocker	5 (56)
ACE inhibitor/ARB	3 (33)
Digoxin	1 (11)
Ivabradine	2 (22)
Oral anticoagulation	7 (78)
Procedure-related medications	
Unfractionated heparin during the procedure	9/9 (100)
Aspirin 300 mg +clopidogrel 300 mg at the beginning of the procedure	9/9 (100)

Values are mean ± SD or n (%). [a]Geometric mean ± SD.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; eGFR = estimated glomerular filtration rate; MRA = mineralocorticoid receptor antagonist; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association.

TABLE 2 Reported SAE Throughout 30 Days' Follow-Up

Procedure Date	Event Date	Anticipated	SAE Narrative	Device Related	Procedure Related	Outcome
January 26, 2018	February 23, 2018	Yes	Patient was electively, admitted for levosimendan infusion; during that hospitalization, worsening heart failure with prolonged hospitalization occurred	Not related	Not related	Resolved
February 11, 2019	February 12, 2019	Yes	Traumatic removal of urinary catheter, which resulted in hematuria	Not related	Not related	Resolved
February 11, 2019	February 22, 2019	Yes	Hematuria	Not related	Not related	Resolved
February 14, 2019	March 9, 2019	Yes	Body weight increase and exacerbation of signs and symptoms of heart failure	Not related	Not related	Resolved
April 22, 2019	May 6, 2019	Yes	*Klebsiella pneumoniae* infection	Not related	Not related	Resolved
November 24, 2019	February 12, 2019	Yes	Advanced respiratory failure ultimately leading to patient death	Not related	Not related	Death
January 16, 2020	January 16, 2020	Yes	Bleeding issue-hematoma in the Swan-Ganz catheter access site in the neck and continuous bleeding at both venous access sites, which resulted in hemoglobin drop	Not related	Probable	Resolved
November 28, 2019	January 15, 2020	No	Ventricular tachycardia	Not related	Not related	Resolved

SAE = serious adverse event.

hemodynamics were measured, including pulmonary artery pressure, right atrial pressure, pulmonary capillary wedge pressure (PCWP) at baseline, during, and at the end of the therapy.

Additional hemodynamic parameters were monitored using Doraya catheter pressure ports, including CVP and iliac pressure (measured below the device). Systolic blood pressure (SBP) was measured according to hospital guidelines.

STATISTICAL ANALYSIS

Continuous variables with a normal distribution are described using the mean ± SD, variables with skewed distribution are described by the geometric mean ± SD, and categorized variables are given as number and percentage. The normality of data distribution was determined by the Shapiro-Wilk test and Lilliefors-Corrected Kolmogorov-Smirnov test. The statistical significance of difference between 2 time points was assessed using either a paired sample *t*-test or chi-square test. Correlations were evaluated by Spearman's test. The mean gradient created by the Doraya catheter during treatment was collected multiple times during the treatment. The assessments were then averaged over time for each patient. Lastly, the overall group mean value was calculated and presented. A P value <0.05 was considered statistically significant. Statistical analyses were performed using the STATISTICA 13 (StatSoft).

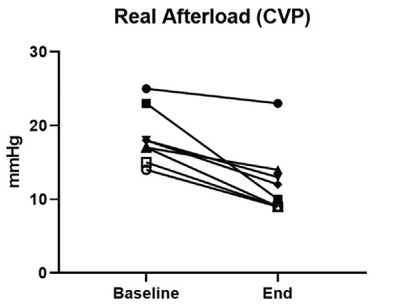
RESULTS

BASELINE CHARACTERISTICS. A total of 9 patients were treated with the Doraya catheter. The study population was predominantly male (n = 7, 78%), with a mean age of 69 ± 9 years and an ischemic etiology of HF in 7 patients (78%). All patients had clinical signs of fluid overload at baseline (Table 1). Moreover, all patients included in the study had a documented insufficient response to diuretic agents, defined by inclusion criteria (see earlier in the text). The mean ± SD creatinine, eGFR, and geometric mean NT-proBNP values at baseline were 2.3 ± 0.7 mg/dL, 31.1 ± 12.4 mL/min/1.73 m^2, and 8,263 ± 8,520 pg/mL, respectively.

Study recruitment was terminated early (after the inclusion of 9 of 15 planned patients) by the sponsor due to the COVID-19 pandemic. The mean time of Doraya catheter placement in the vena cava was 31 ± 27 minutes. The mean time of the procedure (Doraya catheter deployment and creation of pressure gradient in inferior vena cava) was 8.5 ± 1.5 (range 7 to 11.5) hours.

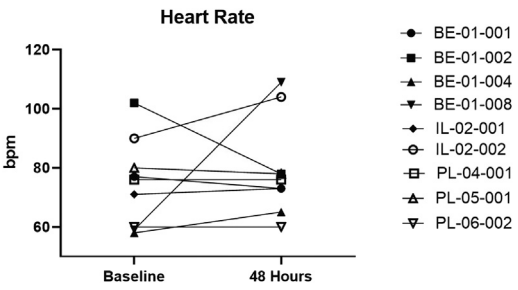
PRIMARY SAFETY ENDPOINTS. Based on independent clinical events committee adjudication, no device-related SAEs were observed during the procedure and within 30 days of follow-up. A total of 8 SAEs were reported during the study (Table 2). One patient experienced a single, probably procedure-related SAE 30 days post-index procedure, consisting of a bleeding hematoma from the Swan-Ganz

FIGURE 2 The Changes in CVP of Individual Patients Before and After the Procedure



CVP = central venous pressure.

FIGURE 3 The Changes in Heart Rate of Individual Patients Before and After the Procedure



Bpm = beats/min.

catheter insertion site, which was resolved without sequelae.

During the 60-day follow-up period, a single patient had a *Klebsiella* infection that was treated with antibiotics and resolved without sequelae. In addition, a single patient had ventricular tachycardia 48 days following the index procedure that was treated with amiodarone and resolved without sequelae. Three subjects (33%) were rehospitalized/experienced worsening HF during the follow-up period. Of these, 2 subjects were rehospitalized for new episodes of AHF and were treated with diuretic agents and resolved without sequelae. The third subject, with several significant comorbidities and advanced HF, deteriorated 10 days after the procedure, while still hospitalized, and ultimately expired.

There were also 22 adverse events reported during the study (up to 60 days), none of which were categorized as device-related. There were no device malfunctions or deficiencies during the study. There were no adverse events defined as catheter thrombosis, catheter misplacement or migration, worsening of lower extremities edema, or other potential complications of elevated venous pressure below the device.

PRIMARY FEASIBILITY ENDPOINTS. The introduction, final placement, and deployment of the Doraya catheter were successful in all study patients. All procedures were technically successful, defined as the ability to position the catheter below the renal veins, regulate the flow in the inferior vena cave, and create the desired pressure gradient of at least 2 mm Hg during the procedure. There were no technical problems during catheter removal.

THE HEMODYNAMIC EFFECT OF THE DORAYA CATHETER IN THE IVC. In all patients, Doraya catheter deployment created a transient and fully controllable gradient in the IVC (below vs above the device), resulting in a decrease of CVP above the catheter during the procedure. The drop in venous pressure was achieved in all study patients: 9 of 9 (100%) (Figure 2). At baseline, the mean pressures in the IVC above and below the catheter were 18.4 ± 3.8 mm Hg and 17.8 ± 4.0 mm Hg, respectively ($P = 0.41$). Following Doraya catheter deployment, the mean pressure in the IVC above the device was significantly lower at 12.4 ± 4.7 mm Hg than the pressure below the device (18.5 ± 6.2 mm Hg; $P < 0.001$). The mean gradient created by the Doraya catheter during the procedure was 4.6 ± 1.1 mm Hg (range 0 to 10 mm Hg across all data points).

THE CENTRAL HEMODYNAMIC EFFECT OF THE CATHETER. During the treatment, the mean CVP decreased from 18.4 ± 3.8 mm Hg to 12.4 ± 4.7 mm Hg ($P < 0.001$), whereas the drop in PCWP did not reach statistical significance (27 ± 5.5 mm Hg to 23.3 ± 9.3 mm Hg; $P = 0.15$). The mean SBP was stable throughout the study period (at baseline, during the procedure, and at the end of the procedure): 112 ± 23 mm Hg, 100 ± 13 mm Hg, and 109 ± 17 mm Hg, respectively. The mean heart rate (at baseline and at the end of the procedure) was 75 ± 15 beats/min and 80 ± 16 beats/min. The individual changes (at the beginning of the study vs 48 hours) of SBP and heart rate of each patient are presented in Figures 3 and 4.

CLINICAL EFFECTS OF DORAYA CATHETER. The baseline mean diuresis, measured 1 day before the procedure, was 77.1 ± 25 mL/h. The mean diuresis increased to 200.8 ± 93 mL/h during device deployment while maintaining at most the same diuretic dose as the baseline. During deployment, the average peak hourly urine output rate was 294 ± 139 mL/h. The mean diuresis increased during the intervention in 7 patients when compared with baseline (Figure 5). Importantly, 1 patient received a higher than baseline

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FIGURE 4 The Changes in Systolic Blood Pressure of Individual Patients Before and 48 Hours After the Procedure

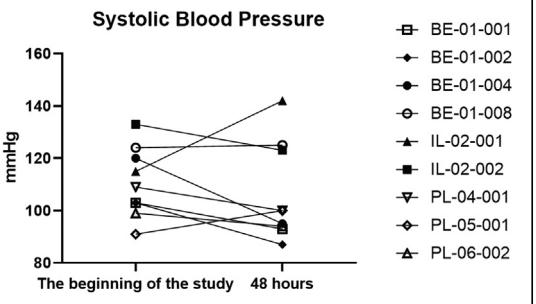
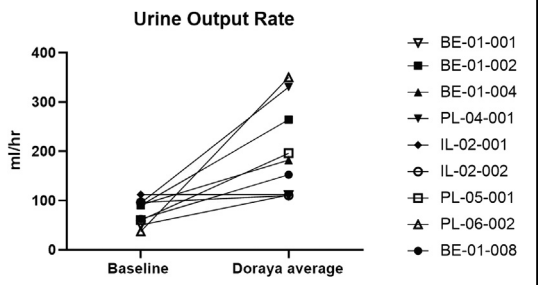


FIGURE 5 The Changes in Urine Output Rate of Individual Patients Before and During the Procedure



dose of diuretic agents during the procedure due to the investigator's decision based on the patient's clinical status. There was also a positive natriuretic signal during the procedure; however, spot urine sodium was measured only in a limited number of patients.

Serum creatinine levels were stable throughout the study. At baseline and 48 hours from Doraya deployment, serum creatinine levels were 2.2 ± 0.7 mg/dL and 2.2 ± 0.9 mg/dL, respectively ($P = 0.70$).

Clinical signs of congestion, namely edema and dyspnea, improved from baseline 1.8 ± 0.8 and −1.4 ± 1.1 to 0.7 ± 0.9 and 1.1 ± 0.9, respectively, postprocedure (48 hours from initiation of the Doraya deployment) (Figures 6 and 7).

The gradient created by catheter deployment was correlated with the patient-reported dyspnea change, defined as the difference at 48 hours postprocedure vs baseline (Spearman's rho = 0.868; $P = 0.025$). The dyspnea change was also correlated with the CVP achieved at the end of the procedure (rho = 0.971; $P = 0.001$). In addition, there was a trend for correlation between edema score improvement and PCWP gradient (defined as the difference between PCWP at the end of the procedure and baseline, Spearman's rho = 0.66; $P = 0.053$).

The liver function tests (namely, albumin and bilirubin) before and after (48 hours) the device implantation were available in 5 patients. There was no change in those markers; the mean albumin (at baseline) was 3.7 ± 0.4 mg/dL vs 3.5 ± 0.4 mg/dL at 48 hours; $P = 0.37$, and bilirubin (at baseline) was 1.7 ± 0.2 mg/dL vs 1.8 ± 0.6 mg/dL at 48 hours; $P = 0.85$.

DISCUSSION

Our study shows that modifying the IVC pressure using the Doraya catheter is feasible and safe in AHF patients. Previous studies demonstrated that elevated CVP is crucial in determining kidney function and predicts poor diuretic response in HF settings.[1,2] Thus, interventions to decrease renal vein pressure are expected to alleviate decongestion. Importantly, Doraya catheter deployment induced a controllable drop of pressure in the IVC with a mean reduction of 6 mm Hg from baseline to procedure end. We predict that this pressure decrease will translate into reduced pressure in renal veins resulting in a better diuretic response. The Doraya catheter provides a unique opportunity to modulate and adjust the venous pressures in conjunction with HF diuretic therapy. Notably, the catheter allows the clinicians to adjust the IVC pressure in real time at the bedside once deployed.

Although the inadequate or even failure in response to diuretic agents in has multidirectional pathophysiology, the elevated CVPs "sensed" by the kidneys are of significant importance.[5] However, this mechanism leads to a vicious cycle: fluid overload leads to neurohormonal activation with subsequent elevation in CVP and impaired renal perfusion, finally resulting in a poor diuretic kidney response. Standard treatment (pharmacotherapy and/or ultrafiltration) is directly aimed at the first 2 cycle components, thereby indirectly affecting the third. The novelty of the Doraya concept is that the catheter directly modifies venous pressure and potentially may break the cycle. This observation indicates that among other causes, the impairment in renal perfusion pressure and flow may contribute to blunt the diuretic and natriuretic responsiveness reported in AHF.[6-9]

Although this first-in-human safety feasibility study was not intended to explore the clinical benefit of the Doraya catheter, some early important clinical observations can be derived from the study. First, the diuretic response to the same dose of diuretics improved during the study intervention period (maintenance of the venous gradient by the catheter

FIGURE 6 The Changes in Dyspnea of Individual Patients Before and 48 Hours After the Procedure

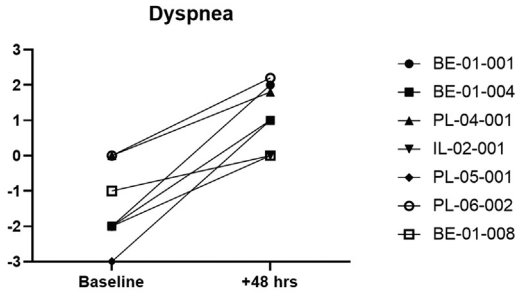
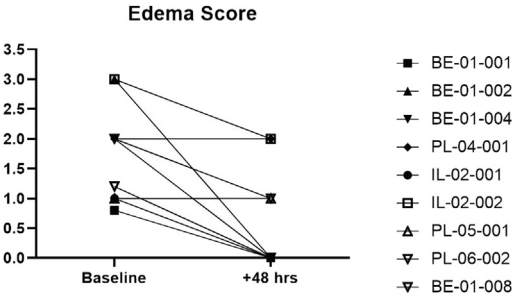


FIGURE 7 The Changes in Edema Score of Individual Patients Before and 48 Hours After the Procedure



and right after). Preliminary results also show improvement in natriuresis (data not shown due to a limited number of patients with spot urine sodium assessments). Second, serum creatinine and eGFR levels were stable in patients undergoing the procedure, which is important from a clinical and safety perspective.[10,11] Third, there was a clear trend of improvement in central hemodynamics after the procedure, namely in CVP and PCWP. This result signified effective decongestion and was indeed accompanied by alleviated clinical symptoms (dyspnea and edema). Moreover, the hemodynamic changes that were observed in the study are in line with other investigators that used different concepts for right ventricle preload control in HF.[12] In early studies, splanchnic nerve blockade resulted in reduction of cardiac filling pressures during exercise (probably through the decrease of stressed blood volume), and improved quality of life and exercise capacity.[12-15] Similarly, in patients with HF and preserved ejection fraction, a transient, titrated partial occlusion of the IVC through balloon inflation during exercise resulted in approximately 25% reduction in pulmonary artery pressure (without deterioration of cardiac output) and improvement in metrics of exercise tolerance.[16,17]

Importantly, catheter deployment was safe, and there were no adverse events related to increased venous pressures below the catheter or embolic events during or following the procedure. The only study-related adverse event, bleeding from the Swan-Ganz catheter implantation site, was not directly related to the catheter itself and resolved without sequelae. Future protocols may consider a less aggressive anticoagulation regime to decrease the risk of bleeding.

This study was conducted on HF patients with poor diuretic response, a high-risk population with advanced HF and renal function deterioration. Thus, these early positive clinical signals demonstrate the potential for future Doraya catheter clinical development. Because present European Society of Cardiology guidelines recommend that decongestion therapy be based on spot urine sodium and urine volume assessments, we can only speculate that interventions on central venous pressure may be beneficial in patients who do not respond adequately to diuretics, however, this needs to be proven in a prospective randomized clinical trial.[10,18]

STUDY LIMITATIONS. The low number of patients enrolled (lower than expected) and the limited duration of the intervention are obvious limitations. Secondly, in this study we were not able to collect some of the important clinical, laboratory, or hemodynamic signals that may be very useful from a pathophysiological perspective. Moreover, the lack of standardized loop diuretic dosing and administration regimen makes the interpretation of the clinical observations more difficult. Theoretically, the Doraya catheter deployment may result in decrease of preload for the right ventricle, which in turn may lead to drop in cardiac output. Unfortunately, we did not routinely measure the cardiac output during the trial, which limits our report. On the other hand, we need to emphasize that the catheter induces the controllable pressure gradient in the IVC, not a total obstruction of the venous flow from the lower extremities. Moreover, we did not observe the systemic, clinical signs of cardiac output drop during the procedure.

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CONCLUSIONS

In this first human use of the Doraya catheter, we have demonstrated that a transient and fully controllable decrease in inferior vena cava pressure is safe and feasible in heart failure patients. Further investigation is needed to determine the clinical applicability of the device.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: This study presents a novel clinical method, the use of a Doraya catheter, which can safely modify inferior vena cava pressure in acute heart failure patients.

TRANSLATIONAL OUTLOOK: Because decreasing renal vein pressure alleviates decongestion, we predict that the Doraya-induced pressure decrease will translate into reduced pressures in renal veins, thereby resulting in improved diuretic response. Therefore, the Doraya catheter may provide a novel modality for modulating and adjusting the venous pressures in conjunction with HF diuretic therapy.

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KEY WORDS acute heart failure, device therapy, diuretic resistance, insufficient response, venous congestion

APPENDIX For an expanded Methods section, please see the online version of this paper.