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STUDY DESIGN

# The role of intra-abdominal pressure and point of care ultrasound to guide decongestive therapies in acute heart failure

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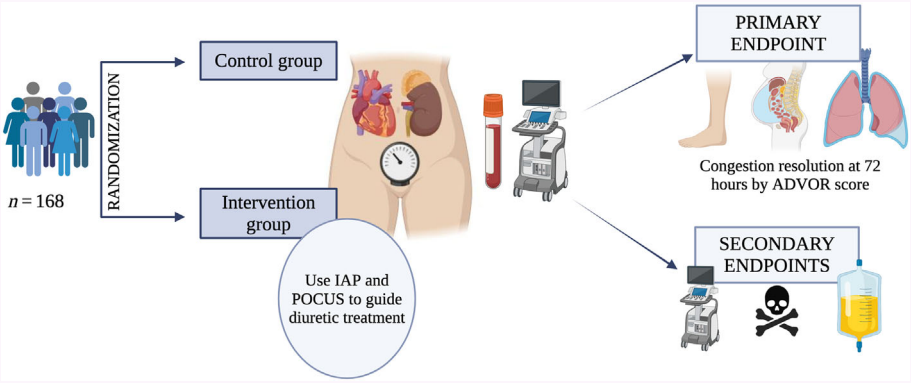
## ABSTRACT

**Aims** Effective decongestion is crucial in managing acute decompensated heart failure (ADHF). Persistent congestion post-diuretic therapy correlates with adverse outcomes. This study evaluates whether a strategy guided by intra-abdominal pressure (IAP) and point-of-care ultrasound (POCUS) enhances decongestion compared to standard diuretic titration.

**Methods and results** ABDOPOCUS-HF is a randomized, multicentre, open-label, pragmatic clinical trial involving 168 patients hospitalized with ADHF across 14 Spanish hospitals. Inclusion criteria encompass clinical signs of congestion and elevated natriuretic peptides (NT-proBNP >1000 pg/mL or BNP > 250 pg/mL). Participants are randomized 1:1 to either standard care or an intervention arm where diuretic therapy is guided by baseline IAP measurements and POCUS assessments, including lung ultrasound, inferior vena cava diameter and VExUS score. The primary endpoint is the resolution of systemic congestion at 72 h, measured by the ADVOR score. Secondary endpoints include changes in pulmonary congestion (B-lines), intravascular congestion (VExUS and IVC), biomarkers (NT-proBNP and CA125), total diuretic dose, diuretic response, hospital length of stay and rates of cardiovascular death, rehospitalization and need for intravenous diuretics at 30 and 90 days. Safety endpoints encompass worsening renal function, electrolyte disturbances and catheter-related infections.

**Conclusions** The ABDOPOCUS-HF trial investigates whether integrating IAP and POCUS into decongestion strategies improves diuretic response and clinical outcomes in ADHF patients. Findings may inform future protocols for volume management in acute heart failure.

## Graphical Abstract




The ABDOPOCUS-HF trial is a randomized, single-blind, low-intervention clinical trial (n = 168) investigating the utility of intra-abdominal pressure (IAP) and point of care ultrasound to guide decongestive therapies during the first 72 hours after admission for acute heart failure. The primary endpoint is significant congestion reduction at 72 hours, assessed through ADVOR score. Secondary outcomes include readmission/cardiovascular death at 90 days and changes in congestion biomarkers (NT-proBNP and CA125) and ultrasound parameters (B-lines, VEXUS score). Safety endpoints include electrolyte disturbances and worsening renal function during admission.

**Keywords** Acute heart failure; Cardio-renal syndrome; Diuretics; Intra-abdominal pressure; Point of care ultrasound

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## Introduction

Congestion is the main therapeutical target in patients with acute decompensated heart failure (ADHF) and intravenous (i.v.) loop diuretics are the standard treatment for congestion relief.[1] However, in one-third of ADHF patients, residual congestion persists, what is linked to worse outcomes.[2] The mechanisms of residual congestion are not well understood. Among their most clinically relevant points are the need to improve the assessment of congestion; and to seek for more efficient and safe diuretic strategies based not only on loop diuretics.[1] In this context, several tools have been proposed to guide diuretic treatment, such as blood biomarkers (natriuretic peptides[3] and carbohydrate antigen 125 (CA125),[4] isolated spot urine analysis, including urine sodium concentrations early after the first dose of i.v. loop diuretic,[5,6] and point of care ultrasound (POCUS).[7,8] Both natriuresis, with the recent publication of the Pragmatic Urinary Sodium-based treatment algorithm in Acute Heart Failure (PUSH-HF) trial,[6] and POCUS, with the role of IVC diameter and lung ultrasound (CAVAL-LUS-HF[8]) trial appear to be promising in this context. Additional studies testing new diuretic strategies, aimed to provide a sequential nephron blockade for improving diuretic response, and defeat diuretic resistance, have recently shown positive results.[9,10]

Intra-abdominal pressure (IAP) is a new actor in the cardio-renal syndrome.[11,12] Intravascular and visceral congestion are linked to a rise in IAP during ADHF in a high proportion of HF patients.[12,13] Furthermore, IAP correlated with other well-known indirect markers of congestion such as CA125 or IVC diameter, and the absence of significant IAP reduction after the first 48 h of decongestive treatment has been linked to worse outcomes.[12] This suggests the usefulness of IAP as a new tool for grading systemic congestion and diuretic titration in ADHF patients.

However, achieving an optimal decongestion requires more accurate tools for the assessment of congestion and safer strategies for diuretic administration, based on either dose scalation or combination of drugs. In this context, we hypothesized that baseline IAP together with POCUS can help clinicians to guide decongestive therapy, based on the combination of increasing doses of i.v. furosemide and oral hydrochlorothiazide as needed.

The role of intra-ABDOminal pressure and Point Of care Ultra-Sound in patients with acute heart failure (ABDOPOCUS-HF) has been designed as a pragmatic clinical trial to assess this novel strategy which has not yet been explored in this clinical scenario.

# Study design

## Participants

ABDOPOCUS-HF is a randomized, multicentre, open-label and pragmatic clinical trial that will evaluate the efficacy of IAP measurement and POCUS for guiding decongestive therapy, compared to standard loop diuretic titration in patients with advanced HF admitted to the Internal Medicine and Cardiology departments of 14 Spanish hospitals (a complete list of hospital participants can be consulted in Appendix S1).

Patients participating in the trial will meet the inclusion criteria shown in *Table 1*. HF diagnosis will be made according to European HF guidelines.[1] Congestive signs and/or symptoms and a significant elevation of natriuretic peptides (NT-proBNP > 1000 pg/mL or BNP > 250 pg/mL) will be required.

All of the participants must sign the informed consent form (Appendix S3).

## Study intervention

Patients will be randomized into two groups. The standard of care group will receive diuretic treatment based on the latest HF guidelines.[1] To minimize heterogeneity of diuretic schedule, a protocol of dosage will be offered, but the last decision for dose adjustment will rely on the clinicians in charge of the patient (Appendix S2).

The clinicians in charge of the conventional treatment group will be blind to intra-abdominal pressure measurements. In the intervention group, a scheduled diuretic treatment combining i.v. furosemide and oral hydrochlorothiazide will be administered according to the IAP value on admission and POCUS parameters (*Figures 1* and *2*).

Treatment with sodium-glucose cotransporter type 2 inhibitors (SGLT2i) will be continued in both groups. In patients naïve to SGLT2i, each clinician will have the last decision to start SGLT2i on admission. Regarding the use of mineralocorticoid receptor blockers, they may be used if the patient is already receiving treatment with them, provided that the outpatient dose is not exceeded and there are no contraindications to their use (such as a significant worsening of renal function and/or hyperkalaemia). Among the patients with low concentration of sodium at admission, the decision to continue or not in the study will rely on individual clinical judgement. Finally, to avoid hypokalaemia, additional oral potassium supplements will be prescribed according to baseline potassium concentrations and its time-line changes during admission.

## Intra-abdominal pressure measurement

Intra-abdominal pressure on admission, as a measure of visceral pressure, will be measured using the indirect vesical catheterization method and the Compass UniversalHg© dispositive (Medline®) (Video S1). According to the latest guidelines from the World Society of Abdominal Compartment Syndrome,[14] normal IAP cut-off is set below 8 mmHg while IAP values of >12 mmHg are considered as intra-abdominal hypertension. Due to the 'grey zone' between 8 and 12 mmHg, and possible confounders such as body mass index (BMI) or abdominal wall surface, an additional parameter (IVC diameter and portal Doppler wave pulse) will be added to complement volume status (*Figure 2*).

**Table 1** Eligibility criteria for ABDOPOCUS-HF low intervention trial

| Inclusion criteria | Exclusion criteria |
|---|---|
| 1. Men or women over the age of 18 years<br>2. Diagnosis of HF based on the latest HF guidelines published in 2021.<br>3. NT-proBNP > 1000 pg/mL or BNP > 250 pg/mL.<br>4. Hospital stay in the Internal Medicine Department < 24 h.<br>5. Placement of bladder catheterization to measure intra-abdominal pressure.<br>6. Intravascular or mixed congestion pattern, defined as the presence of one or more clinical signs of congestion (oedema, ascites and/or pleural effusion).<br>7. Informed consent signed. | 1. Insufficient clinical congestion (ADVOR score = 0 at the time of randomization).<br>2. Patient's refusal to participate in the clinical trial.<br>3. Inability or contraindication for the placement of a bladder catheter.<br>4. Systolic blood pressure at the time of admission < 100 mmHg.<br>5. Heart rate at admission > 170 beats per minute (b.p.m.).<br>6. Cardiogenic shock.<br>7. Acute myocardial ischaemia.<br>8. Patients receiving renal replacement therapy (ultrafiltration or peritoneal dialysis).<br>9. Kidney transplant recipients.<br>10. Serum haemoglobin < 9 g/dL.<br>11. Pregnancy or lactation.<br>12. Previous history of hypersensitivity to hydrochlorothiazide or furosemide.<br>13. Patients whose origin is the Intensive Care Unit.<br>14. Patients with recent cardiac surgery (last year) or heart transplant recipients.<br>15. Need for inotropic support to maintain adequate cardiac and/or renal output. |

BNP, b-type natriuretic peptide; HF: heart failure; NT-proBNP, N-terminal pro b-type natriuretic peptide.


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**Figure 1** Protocol and outcomes. IAP, intra-abdominal pressure; i.v., intravenous; ivc, inferior vena cava; LUS, lung ultrasound; POCUS, point of care ultrasound; VeXuS, venous excess ultrasound protocol.

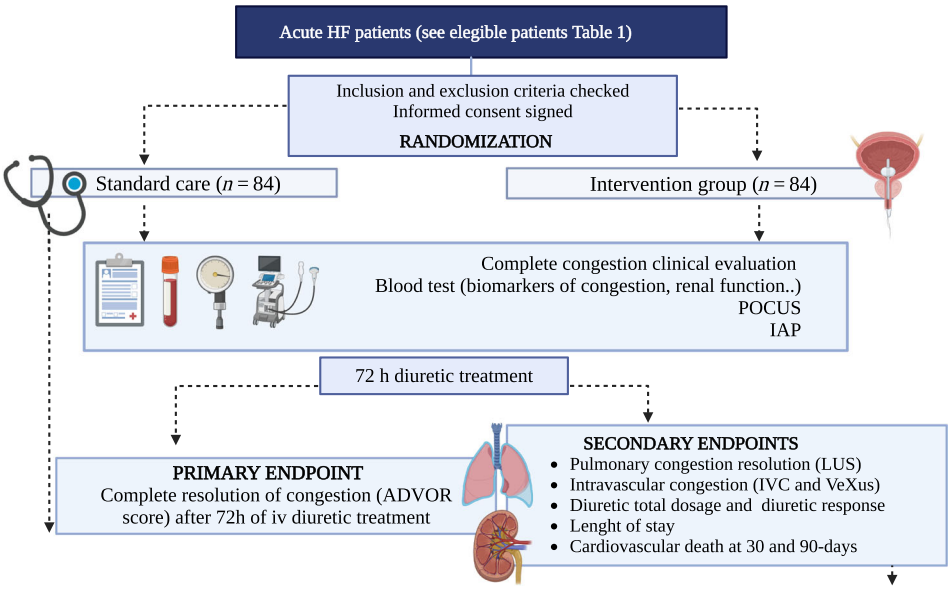
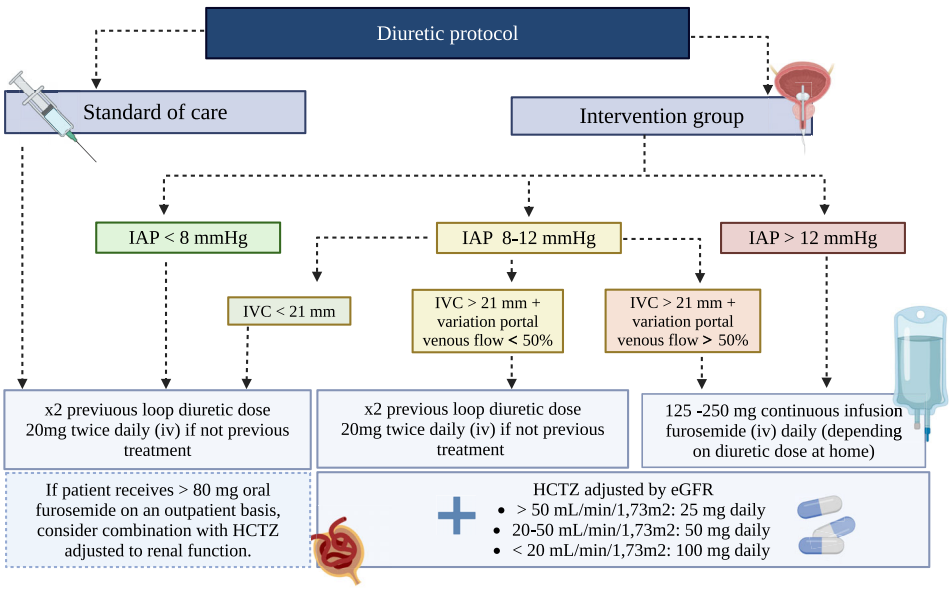



**Figure 2** Diuretic protocol. eGFR, estimated glomerular filtration rate; IAP, intra-abdominal pressure; iv, intravenous; IVC, inferior vena cava.




## Multimodal assessment of congestion and diuretic response quantification

At randomization, a complete congestion clinical evaluation will be performed, encompassing jugular vein distension (JVD), orthopnoea, oedemas, pleural effusion (it will be quantified based on the distance between the lung and the diaphragm. Pleural effusion will be considered non-significant or non-puncturable if it is <1 cm, and significant or puncturable if it is greater than 1 cm), and ascites quantification (ADVOR-score[10]). Serum biomarkers of congestion (CA125 and NT-proBNP) and POCUS (lung ultrasound, analysis of IVC diameter and VeXuS score)[2,3,7,8] will also be acquired, following current image guidelines.[15] Regarding lung ultrasound (LUS), within the first 24 h of admission, a bedside thoracic ultrasound will be performed to identify and quan-

tify B-lines. The same experienced physician will carry out all LUS examinations with the patient reclined at 30 degrees. Both the anterior and lateral hemi-thorax will be divided into upper or lower quadrants, resulting in eight quadrants in all. B-lines are narrow, vertical, bilateral and diffuse linear echogenic images visualized from the 2nd to 4th intercostal spaces, which reflect differences in acoustic impedance in the lungs. A positive assessment is defined as >3 B-lines per area in at least two areas per hemi-thorax.

Diuretic response will be estimated through the total diuresis during the first 72 h, along with an isolated spot urine analysis 2 h after the first dose of i.v. furosemide. The total dosage of diuretics will be registered along with ordinary renal function parameters, including estimated glomerular filtration rate (eGFR) by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) based on creatinine (mL/min/1.73 $m^2$), and microalbuminuria/creatinine ratio (mg/g). Impaired renal function will be defined as eGFR < 60 mL/min/1.73 $m^2$ or eGFR ≥ 60 mL/min/1.73 $m^2$ plus the presence of significant microalbuminuria (>30 mg/g).

## Study endpoints

The primary endpoint of the ABDOPOCUS-HF trial will be the significant congestion resolution after the first 72 h of diuretic treatment measured through ADVOR score between both groups (*Figure 1*).[10] Secondary endpoints include (a) pulmonary congestion resolution as estimated by means of B-lines (LUS) after 72 h; (b) reduction of intravascular congestion (inferior vena cava diameter and VExUS protocol) after 72 h; (c) reduction of intravascular congestion biomarkers, determined by NT-proBNP measured at admission, discharge and first outpatient visit; (d) reduction of tissue congestion, measured through CA 125, on admission, discharge, and first outpatient visit; (e) variation in IAP between admission and the 72 h following it; (f) total diuretic doses administered and g) diuretic response after 72 h; (h) in-hospital length of stay; (i) weight change after the first 72 h; (j) cardiovascular death at 30 and 90 days; (k) HF-rehospitalization at 30 and 90 days; (l) need for i.v. furosemide at 30 and 90 days and (m) combined end-point of cardiovascular death, HF-rehospitalization and need for i.v. furosemide at 30 and 90 days. Safety endpoints will include: worsening renal function (defined as an increase of 0.3 mg/dL or more in creatinine at any time during hospital admission), urinary tract infections due to urine catheter placement and ionic alterations clinically relevant related to the use of i.v. diuretics (hyponatremia < 135 mmol/L, hypokalaemia < 3.5 mmol/L or hyperkalaemia > 5.1 mmol/L) and due to excessive diuresis and volume contraction, as hypernatremia > 145 mmol/L and metabolic alkalosis (blood pH > 7.45 with bicarbonate > 26 mEq/L).

## Secondary analyses

Our intention is to conduct a sub-analysis later based on several parameters: (1) IAP at admission, (2) ejection fraction (reduced, moderately reduced, and preserved), (3) renal function at admission with eGFR above or below 60 mL/min/1.73 $m^2$, (4) natriuresis above or below 70, (5) according to the presence or absence of normal or low blood pressure and (6) according to gender.

## Follow-up

After randomization, diuretic treatment will be started and continued according to protocol during the first 72 h (*Figure 2*). In both groups, an additional total dose of i.v. furosemide of 40 mg will be allowed during the first 72 h of randomization as a 'rescue' treatment. Any other situation that requires a diuretic adjustment will not be allowed. In contrast, fast i.v. furosemide down-titration to oral furosemide before 72 h will be allowed and registered. After 72 h of diuretic treatment, a complete congestion assessment (control visit) will be performed, and individual decisions for vesical catheter removal will be taken by each physician. In this phase, the total dose of diuretics and total diuresis will be also registered. After the control visit, consecutive visits at discharge, and HF-clinics will be performed until 90 days (*Figure 3*).

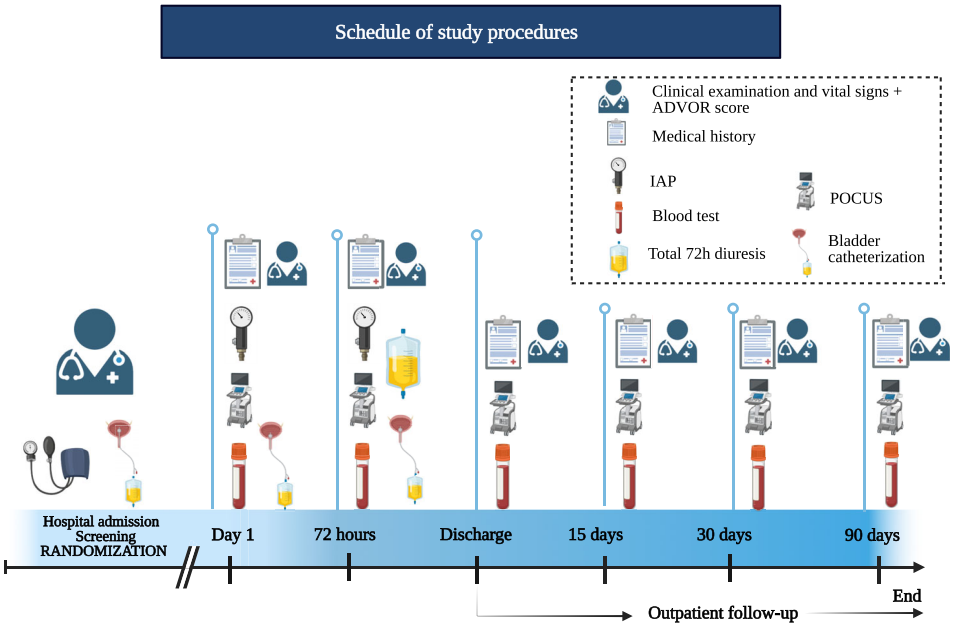
## Statistical plan and sample size

According to previous clinical trials related to decongestive therapy in patients with ADHF,[10] a total sample of 168 patients was calculated with 84 patients in each group. (Parameters used for the sample size: alpha error 0.05; bilateral contrast; beta risk 0.20; congestion proportion after the first 72 h: Group 1 42%, Congestion proportion after the first 72 h intervention group 21%; ratio of subjects between groups 1:1; expected proportion of losses to follow-up 10%. The sample size did not require adjustment due to the gender perspective).

Randomization will be performed by an independent informatic programme, included inside the online database design specifically for the ABDOPOCUS-HF trial by 'pInvestiga, L.S.' (https://www.pinvestiga.com/). To avoid bias, gender and the presence of impaired renal function (eGFR < 60 mL/min/1.73 $m^2$) on admission will be considered for randomization.

Qualitative variables will be expressed as numbers and percentages and quantitative variables as mean ± standard deviation or median (interquartile range), depending on whether they follow normality. For hypothesis contrast, the Student's *t*/Mann–Whitney *U* test and the

**Figure 3** Schedule of study procedures. IAP, intra-abdominal pressure; POCUS, point of care ultrasound.




chi-square test will be used as appropriate. The survival curves will then be analysed using Kaplan–Meier curves and the long-rank test for the combined secondary variable of cardiovascular death/readmission for HF/need for intravenous diuretic in the day hospital. A univariate and multivariate analysis will also be performed using Cox regression to identify those variables that predict the secondary objective. For this analysis, those variables that are significant in the univariate analysis, those with biological plausibility or that have been previously identified in the literature, and those with a $P < 0.100$ in the univariate analysis will be considered. A level of significance will be considered when the $P$ value is $<0.05$.

All events will be recorded in the database and will later be evaluated by an independent committee.

## Ethical and administrative considerations

The trial has been approved by the Comité Ético de Investigación Clínica de Aragón (CEICA), protocol number PI23/00797–1.0. Version; approved (24 July 2024) in Spain, and will be conducted following the Declaration of Helsinki and the International Conference of Harmonization Guidelines for Good Clinical Practice. All participants will provide written informed consent. The trial has been registered and approved at the Clinical Trials European Union (CTIS) (EU CT Number: 2024-512901-22-00) and ClinicalTrials.gov (NCT07008365). Pharmaceutical monitoring and vigilance will be performed by 'O.C.vigilance L.S.' (https://www.ocvigilance.com/).

# Discussion

The ABDOPOCUS-HF clinical trial is a single-blind, randomized, pragmatic study aimed to assessing the utility of guiding a combined diuretic strategy (furosemide + hydrochlorothiazide) based on IAP and POCUS data upon admission for ADHF. The trial design will also allow for multiple analysis of congestion progression and a detailed study of urinary metrics, as patients will remain catheterized (vesical catheter) during the period of maximal exposure to diuretics following admission (first 72 h).

## Congestion and intra-abdominal pressure in cardio-renal syndrome

The concept of congestion in patients with HF has evolved significantly over the years. While it is true that congestion remains the primary therapeutic target of loop diuretics, growing evidence highlights the physio-pathological mechanisms by which persistent congestion can harm HF patients.[16] Retrospective studies have shown that sustained increases in central venous pressure (CVP) correlate with worse medium-term prognosis, but also that this parameter plays a more critical role in cardio-renal syndrome than ischaemia, as was previously thought.[17] Indeed, congestive nephropathy is present in a large proportion of patients with ADHF and explains why, in some cases, intensive diuretic therapy can lead to renal function improvement in certain cases (worsening and pseudo-worsening renal function).[18,19] This fact, along with advances in congestion assessment, such as the venous

excess ultrasound protocol (VEXUS),[20] enhances our understanding of congestive nephropathy and opens the door to new decongestive treatment strategies.

Although congestion can impair renal function in HF patients, understanding the precise physio-pathological mechanisms behind this process remains challenging. In this context, IAP appears to play a role.[13,14] The abdominal cavity is an enclosed compartment, bordered by the diaphragm, abdominal wall muscles, and pelvic floor. The kidneys, located in the retroperitoneum and surrounded by a significant fat layer, are perfused by the renal arteries at a constant filtration rate, which depends, among other factors, on IAP.[21] Studies in critically ill patients[13] have demonstrated that a significant and sustained increase in this parameter can reduce renal perfusion pressure and glomerular filtration rate.

In HF patients, sustained activation of the sympathetic nervous system can lead to dysregulation of the splanchnic venous abdominal bed. This situation combined with visceral venous congestion and the kidneys inability to expand due to its confinement within a fatty compartment, can lead to damage in renal structures. Animal models of ADFH with pulmonary hypertension have shown the presence of plasma and urinary markers of tubular dysfunction in the presence of elevated IAP.[22] Furthermore, multiple studies in patients with advanced HF have demonstrated that a high proportion of patients exhibit elevated IAP, which correlates with objective measures of congestion, such as CA125 levels or IVC diameter—both routinely used in the management of patients with ADHF.[23]

Thus, IAP plays a dual role in cardio-renal syndrome: it acts as a physio pathological mechanism capable of damaging renal structures, but it also serves as a potential tool for measuring congestion during hospitalization, with the notable advantage that this parameter can be measured by standardized devices, as occurs with CVP, but in an easier and safety way (only needs for vesical catheterization, a technique normally used during ADHF assistance that can be performed by nurses). This situation can reduce inter-observer variability seen with other techniques, such as POCUS or natriuresis, which may be influenced by prior treatments or pre-existing comorbidities—a common situation in HF patients, particularly those with heart failure with preserved ejection fraction (HFpEF).

In summary, according to our hypothesis, IAP could have a practical clinical value beyond being a mere physiopathological mechanism of congestive nephropathy.

## Treatment of congestion in heart failure: A paradigm shift?

As we have previously discussed, congestion plays a complex and crucial role in HF patients. This may explain why diuretic strategies based solely on physical examination and monotherapy with intravenous loop diuretics have a high failure rate, particularly in patients with chronic kidney disease (CKD) and long-standing heart conditions.[2]

In response to these outcomes, the scientific community has developed various strategies to improve results, primarily by a better categorization of the patient's congestive state, but also by introducing novel diuretic strategies, where drug combinations have gained prominence. In this regard, the advent of POCUS, in combination with natriuretic peptide levels and CA125, is crucial in identifying the different congestive patterns in HF patients.[24] This allows for the individualization of diuretic strategies depending on whether congestion is predominantly pulmonary tissue-based or intravascular, where higher doses of diuretics are required. However, determining the appropriate diuretic dosage and the rate at which to escalate treatment is more complex. Urinary metrics analysis, particularly urinary sodium concentrations within the first 2 h of intravenous loop diuretic administration, has emerged as a valid strategy for clinical practice. Initial observational studies showed that patients with a natriuretic response below 50–70 mmol/L after the first diuretic dose had a poorer prognosis.[6] This observation led to clinical trials validating this treatment strategy in patients with acute heart failure, specifically the Efficacy of a Standardized Diuretic Protocol in Acute Heart Failure (ENACT-HF[25]) and The Pragmatic Urinary Sodium-based treatment algorithm in Acute Heart Failure (PUSH-AHF)[6] trials, with similar conclusive results: guiding diuretic therapy based on urinary sodium is safe, more efficient, and enables faster decongestion in ADHF patients, which translates into shorter hospital stays.

However, achieving a sustained natriuretic response is often challenging due to the high comorbidity burden in HF patients, particularly those with CKD.[2] In these cases, overcoming diuretic resistance often requires high doses of diuretics, with associated risks and complications. As a result, alternative diuretic strategies have been proposed in recent years, specifically combined diuretic therapies and the use of SGLT2i inhibitors.[26] The safety and Efficacy of the Combination of Loop with Thiazide-type Diuretics in Patients with Decompensated Heart Failure (CLOROTIC trial[9]) demonstrated that combined diuretic treatment with hydrochlorothiazide in patients with previous high-dose oral furosemide treatment (≥80 mg) was safety and effective, increasing diuretic response compared to intravenous furosemide monotherapy. These results held regardless of baseline glomerular filtration rate or left ventricular ejection fraction (LVEF).[27] Additionally, the Acetazolamide in Decompensated Heart Failure with Volume Overload trial (ADVOR)[10] investigated the combination of loop diuretics with intravenous acetazolamide versus standard loop diuretic therapy, demonstrating that the combination with acetazolamide was superior to monotherapy. Both trials have introduced new approaches to managing congestion in patients with ADHF, though each with its specificities.

In this study, we opted for hydrochlorothiazide primarily for two reasons: first, intravenous acetazolamide is not avail-

able in Spain, and second, the patient profile in the CLOROTIC trial was the same as that in the ABDOPOCUS-HF trial. Therefore, this study will provide deeper insight into the utility of a combined diuretic strategy with hydrochlorothiazide, but applied differently, based on objective congestion parameters (IAP and POCUS) rather than on diuretic doses used before admission.

### Limitations

It will be considered as a limitation the possible intra- and inter-observer variability regarding the POCUS measurements and intra-abdominal pressure.

## Acknowledgements

We thank the staff of MEDLINE for their assistance in the distribution and the necessary training to perform intra-abdominal pressure measurements.

## Conflict of interest

The authors declare no conflicts of interest.

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## Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Appendix S1.** List of hostpital participants.
***Appendix S2.*** *Suggested diuretic protocol based on latest recommendations of HF guidelines.*
***Appendix S3.*** *Withdrawal criteria.*
***Video S1.*** *Introducing compass: Intra-abdominal pressure monitoring kit.*

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