



VExUS-ED: Early venous congestion is associated with clinical fluid overload in patients with sepsis

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ABSTRACT

Background: Initial fluid resuscitation is central to sepsis management, yet excessive fluids may exceed a patient's fluid tolerance, increasing the risk of fluid overload and organ dysfunction. The Venous Excess Ultrasound (VExUS) score allows noninvasive bedside assessment of venous congestion, but its prevalence and predictive value in the emergency department (ED) are unclear.

Methods: We analyzed prospectively collected data from the Acutelines data-biobank (University Medical Center Groningen, Netherlands). Adults with suspected sepsis requiring initial fluid resuscitation underwent VExUS assessments, including inferior vena cava and organ-specific Doppler measurements, within three hours of ED admission. The primary outcome was clinical fluid overload within 72 h, defined as positive fluid balance plus $\geq 10\%$ weight gain, pulmonary edema on imaging, or loop diuretic use. Associations were analyzed using logistic and mixed-effects regression.

Results: Among 103 patients, 34 (33%) developed clinical fluid overload. At ED admission, 75% had VExUS grade 0, 22% grade 1, and 3% grade ≥ 2 . At baseline, VExUS >0 and abnormal hepatic venous Doppler flow were associated with fluid overload within 72 h (aOR 3.66, 95% CI 1.23–11.55; $p = 0.022$ and 4.20, 95% CI 1.21–16.38; $p = 0.028$, respectively). In repeated-measures analyses, VExUS >0 and abnormal intrarenal venous Doppler flow were associated with next-day fluid overload.

Conclusion: In patients with suspected sepsis, mild venous congestion was independently associated with clinical fluid overload within 72 h. Abnormal hepatic and intrarenal flow patterns may provide additional information on venous congestion. Early, serial VExUS assessments may detect fluid intolerance and support individualized fluid management.

List of abbreviations

AVPU	Alert, Verbal, Pain, Unresponsive
BMI	Body Mass Index
BLUE	Bedside Lung Ultrasound in Emergency
CI	Confidence Interval
CRRT	Continuous Renal Replacement Therapy
ED	Emergency Department

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EPA	Entrustable Professional Activity
ESICM	European Society of Intensive Care Medicine
HV	Hepatic Vein
ICU	Intensive Care Unit
IQR	Interquartile Range
IRB	Institutional Review Board
IRV	Intrarenal Vein

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IV	Intravenous
IVC	Inferior Vena Cava
MAP	Mean Arterial Pressure
MEWS	Modified Early Warning Score
OR	Odds Ratio
PoCUS	Point-of-Care Ultrasound
PV	Portal Vein
PWD	Pulse Wave Doppler
RAP	Right Atrial Pressure
SBP	Systolic Blood Pressure
SIRS	Systemic Inflammatory Response Syndrome
SOFA	Sequential Organ Failure Assessment
UO	Ultrasound Operator
UMCG	University Medical Centre Groningen
VExUS	Venous Excess Ultrasound

1. Introduction

Current sepsis management relies on standardized, guideline-driven resuscitation pathways, with early hemodynamic resuscitation that primarily involves fluid administration and, when indicated, vasopressor support, in addition to timely antimicrobial therapy and source control (1). Existing sepsis guidelines recommend early administration of large volumes of crystalloid fluids in patients with sepsis-induced hypoperfusion or septic shock to improve cardiac output and organ perfusion (2,3).

However, fluid therapy carries risks, and over-resuscitation may be harmful in sepsis. Volume overload, amplified by septic cardiomyopathy, vasodilation, and increased vascular permeability, can promote venous congestion and secondary organ injury (4–8). Although dynamic assessments of fluid responsiveness help guide fluid administration, they do not indicate a patient's ability to tolerate volume expansion (9,10). The emerging concept of fluid tolerance describes the extent to which volume administration can occur without causing organ dysfunction (10). Notably, venous congestion may occur even in fluid-responsive patients (11), underscoring the need for an individualized resuscitation strategy that balances fluid responsiveness and tolerance (12).

Early recognition of venous congestion can guide initial fluid resuscitation in the emergency department (ED). Venous congestion can be directly assessed at the bedside using point-of-care ultrasound (PoCUS) (13,14). The Venous Excess Ultrasound (VExUS) grading system provides a structured, noninvasive approach to quantify systemic venous congestion, a marker of fluid tolerance, by integrating inferior vena cava size (IVC) and Pulse Wave Doppler patterns of hepatic, portal, and intrarenal veins (9,13). VExUS has mainly been studied in intensive care populations, with mixed results, likely due to advanced disease severity, profound hemodynamic impairment, and extensive prior fluid loading (15–20). In contrast, the ED offers an opportunity to assess VExUS earlier in the disease course, before venous congestion or organ dysfunction develops.

Therefore, the primary objective of this study is to evaluate the prevalence of VExUS grades in the ED and early post-ED period and to assess their association with the development of clinical fluid overload within 72 h in patients with suspected sepsis requiring intravenous (IV) fluid resuscitation. Secondarily, we assessed whether abnormalities in individual venous Doppler components, including hepatic, portal, and intrarenal vein flow patterns, were associated with subsequent fluid overload. We hypothesize that VExUS and its individual components could serve as an early, rapid, noninvasive, and cost-effective marker of venous congestion, with the potential to identify patients at risk of fluid overload and thereby supporting more personalized fluid management strategies.

2. Methods

2.1. Study design

We conducted a post-hoc analysis of prospectively obtained data by Acutelines: a data-, image- and biobank at the ED of the University Medical Center Groningen (UMCG) (21). A deferred consent procedure (by proxy) was in place to enable the collection of data and biomaterials before obtaining written consent. When reaching the patient or proxy was not feasible, we followed an opt-out procedure. Acutelines is approved by the medical ethics board of the UMCG and registered under trial registration number NCT04615065 at ClinicalTrials.gov. The study protocol was approved by the institutional review board (IRB) under registration number 21256. Acutelines' complete protocol and overview of the actual, entire data dictionary is available via www.acutelines.nl (21).

2.2. Study population

Between October 1, 2024, and June 1, 2025, consecutive adult patients (≥ 18 years) presenting to the ED were screened. Eligible patients had a suspected or confirmed early sepsis, determined by the treating physician or ED nurse using predefined criteria (qSOFA ≥ 2 , SIRS ≥ 2 , temperature $< 36^\circ\text{C}$ or $> 38^\circ\text{C}$ and/or blood cultures taken) and required initial fluid resuscitation in the ED. Indications for fluid resuscitation included at least one of the following, first measured pre-hospital or at ED triage: heart rate > 100 beats/min, mean arterial pressure (MAP) < 70 mmHg, a systolic blood pressure (SBP) < 90 mmHg or a > 40 mmHg decrease from baseline, a shock index (heart rate/SBP) > 0.9 , or blood lactate > 4 mmol/L.

Patients were excluded if transferred from another hospital after the initiation of therapy, had hemorrhagic shock, or sustained traumatic injury. For the final analysis, patients were required to have baseline PoCUS measurements in the ED and at least one follow-up assessment on days 1–3. Those with fewer than two assessable VExUS components after image review (Section 2.5) were excluded.

2.3. Outcomes

The primary endpoint was clinical fluid overload within 72 h, defined as a composite of positive net fluid balance and at least one of the following: $\geq 10\%$ weight gain, pulmonary edema on lung ultrasound (bilateral B-lines) or chest X-ray, or loop diuretic use. Secondary endpoints include an increase in Sequential Organ Failure Assessment (SOFA) score > 2 points, ICU admission, need for organ support therapies (vasopressor support, mechanical ventilation, or CRRT) within 72 h, and mortality at 72 h and 30 days.

2.4. Data collection and study procedures

Research assistants screened and enrolled eligible patients at ED triage. After inclusion, trained ultrasound operators (UOs) performed PoCUS to quantify venous congestion, including inferior vena cava (IVC) measurements and pulse wave Doppler (PWD) assessment of the hepatic (HV), portal (PV), and intrarenal (IRV) veins for VExUS evaluation (Fig. 1). All Doppler measurements were evaluated irrespective of IVC size. Lung ultrasound was performed at six locations according to the Bedside Lung Ultrasound in Emergency (BLUE) protocol. Detailed ultrasound procedures are provided in the [Supplemental S1: VExUS-ED US protocol](#). Examinations were performed using Xpore, Sonosite LX, or GE Venue R1 ultrasound systems.

Repeated measures were obtained within three hours of ED admission (day 0) and on days 1, 2, and 3, including vital signs (e.g. noninvasive blood pressure, heart rate, capillary refill time), IV fluid administration, fluid balance, and daily weight. Additional data included on radiological findings, and use of vasopressors, and loop

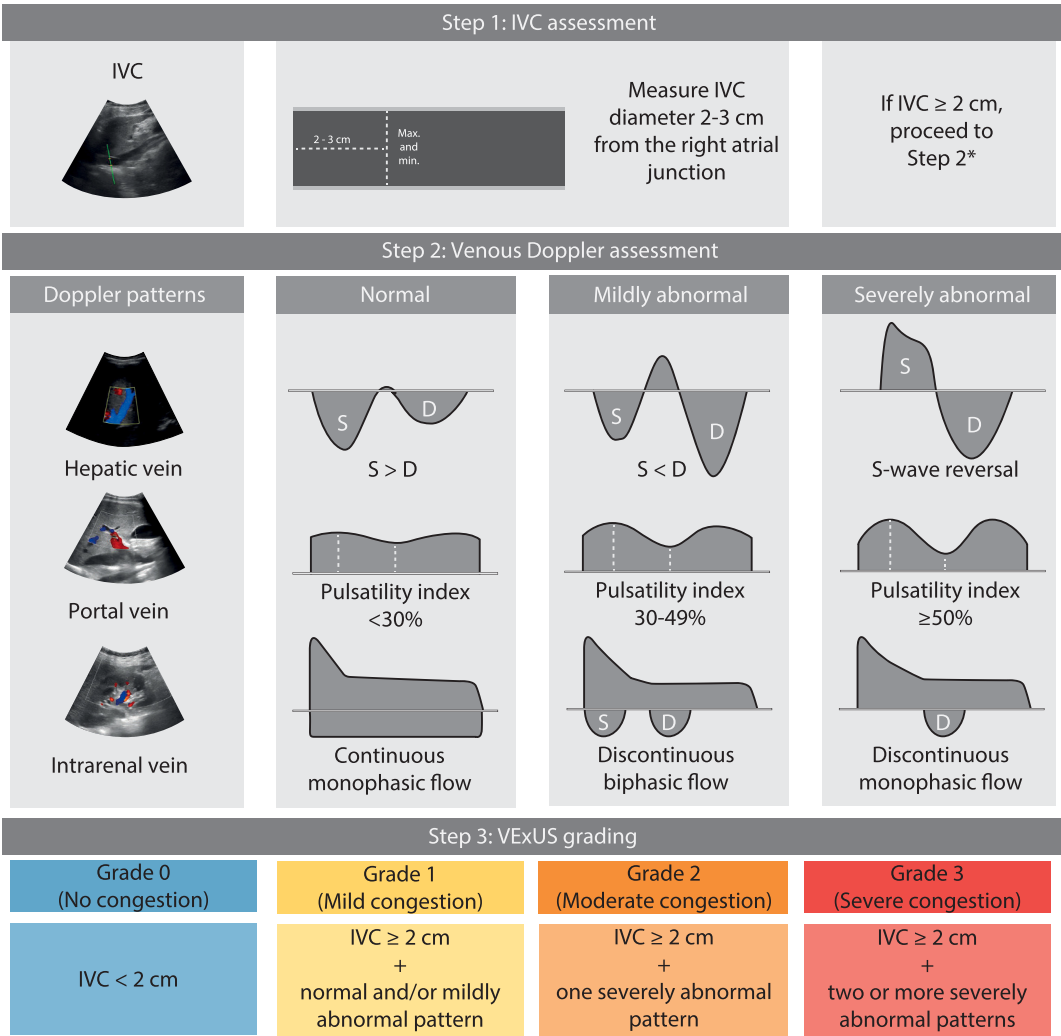


Fig. 1. Overview of the VExUS (Venous Excess Ultrasound) scoring system and interpretation of its individual components. The figure illustrates the evaluation of venous congestion using the Inferior Vena Cava (IVC) diameter and pulse wave Doppler waveforms of the Hepatic Vein (HV), Portal Vein (PV), and Intrarenal Vein (IRV). The pulsatility index is calculated as $(V_{\max} - V_{\min})/V_{\max}$, where V represents velocity. *Step 2 is performed despite of IVC diameter. IVC: inferior vena cava; S: systolic wave; D: diastolic wave; V: Velocity.

diuretics. Demographic and clinical data were collected from the Acutelines databank, including age, gender, comorbidities, in-hospital medication use, height, laboratory values, organ support treatments (cardiac, pulmonary, and renal), and sepsis severity scores (modified early warning score (MEWS), SOFA, quick SOFA (qSOFA)).

2.5. Image quality control and review process

UOs received structured training in VExUS and the BLUE protocol, consisting of literature review, instructional videos, three dedicated training sessions, and initial supervised practice at the start of the study. Upon successful completion, the trainees reached an Entrustable Professional Activity (EPA) level of 3–4, reflecting competence to perform ultrasonography under indirect supervision (22).

VExUS and BLUE images were independently reviewed according to predefined criteria by an independent expert with an EPA level of 4 or higher (see Supplemental S2: VExUS-ED US Review Criteria). Bilateral B-lines were interpreted in clinical context to distinguish pulmonary edema from alternative causes such as pneumonia, using clinical and radiological information. In case of disagreement, a second independent expert adjudicated, with consensus reached during plenary review when required.

2.6. Venous excess ultrasound score

VExUS scores were calculated from IVC and PWD measurements of the HV, PV, and IRV (Fig. 1). Grading was defined as: grade 0: IVC < 2 cm; grade 1: IVC ≥ 2 cm with normal or one mildly abnormal PWD; grade 2: IVC ≥ 2 cm with one severely abnormal PWD; grade 3: IVC ≥ 2 cm with two or more severely abnormal PWD patterns.

2.7. Statistical analysis

Statistical analyses were performed in R (version 4.5.1). Normality of continuous variables was assessed using the Shapiro-Wilk test. Continuous variables were presented as a median (IQR) and categorical variables as counts and percentages. Group comparisons used *t*-tests or Mann-Whitney *U* tests, as appropriate, and chi-squared test for categorical data. Statistical significance was defined as $p < 0.05$. No formal sample size calculation was performed. All eligible patients were included.

A prespecified missing data threshold of 40% was applied. When missingness was below this threshold, multiple imputation was performed using the MICE package, with ordinal VExUS components imputed using proportional odds logistic regression (23). Ten imputed datasets were generated and pooled using Rubin's rules. Given that

missing VExUS scores were considered likely missing not at random (MNAR) due to inadequate image quality in more severely ill patients, best-case and worst-case sensitivity analyses were performed.

Logistic regression analyses were performed to investigate associations between VExUS, and individual components measured at baseline and clinical fluid overload within 72 h. Mixed-effects logistic regression accounted for repeated measurements to evaluate associations with clinical fluid overload within the next 24 h, incorporating patient-level effects. Models were adjusted for patient-specific covariates, including age, sex, and comorbidity burden (Charlson Comorbidity Index (CCI) score). Feasibility analysis examined potential factors associated with missing VExUS scores, and interrater agreement was quantified using Cohen's Kappa.

3. Results

3.1. Study population

Of 182 eligible patients, 123 had baseline and follow-up measurements. After image quality review, 20 patients were excluded, resulting in a final cohort of 103 patients (Fig. 2). Median age of 64 years [IQR 51–72], and 49 (47%) were female. Relevant comorbidities included heart failure (5%), chronic liver disease (5%), chronic kidney disease (18%), and prior kidney (8%) or liver transplantation (4%). Median MAP was 89 mmHg [79–101], heart rate 110 beats/min [104–122], and blood gas lactate 1.6 mmol/L [1.0–2.1]. Median MEWS and SOFA scores were 8 [6–10] and 3 [2–4], respectively. Patients received a median of

1.0 L IV fluids [0.5–1.5], with one patient (1%) requiring vasopressors in the ED. ICU admission occurred in seven patients (7%), of whom four (4%) required vasopressor therapy and four (4%) required mechanical ventilation within 72 h. No patients required CRRT. Median hospital length-of-stay was 5.6 days [3.2–12.4]. Baseline characteristics are summarized in Table 1 and Supplementary Table 1.

The prevalence of VExUS grades and individual components is shown in Table 2. VExUS grade ≥ 2 was uncommon. Most patients classified as grade 0 (75%) or 1 (22%), and only three patients (3%) reaching grades 2–3. The most frequent severely abnormal waveform was HV S-wave reversal (9%), followed by PV pulsatility index $\geq 50\%$ (7%). Severely abnormal IRV flow patterns (discontinuous monophasic) were not observed at baseline, whereas mildly abnormal flow patterns (discontinuous biphasic) were present in 13% of patients. The proportion of patients with VExUS >0 peaked on day 2 (46%). MAP remained largely stable, while heart rate and MEWS scores declined modestly. Cumulative fluid balance and body weight increased modestly. Longitudinal data for patients with complete measurements on day 1–3 ($n = 54$) are presented in Supplementary Table 2.

3.2. VExUS scoring and development of clinical fluid overload within 72 h

Among the 103 patients, 34 (33%) developed clinical fluid overload

Table 1
Baseline characteristics of the study population.

Characteristics of the study cohort	N = 103
Demographics	
Female (n (%))	49 (47)
Age (median [IQR])	64 [51, 72]
BMI (median [IQR])	25.3 [22.5, 28.4]
Co-morbidities	
Charlson Comorbidity Index (median [IQR])	4 [2, 6]
Pre-existent heart failure (n (%))	5 (5)
Chronic kidney disease (n (%))	19 (18)
Chronic liver disease (n (%))	5 (5)
Kidney transplantation (n (%))	8 (8)
Liver transplantation (n (%))	4 (4)
Vital parameters at triage	
Systolic blood pressure [mmHg] (median [IQR])	118 [104, 136]
Mean arterial blood pressure [mmHg] (median [IQR])	89 [79, 101]
Heart rate [beats/min] (median [IQR])	110 [104, 122]
Respiratory frequency [/min] (median [IQR])	20 [16, 24]
Temperature (°C) (median [IQR])	37.2 [36.7, 38.3]
Lab values at triage	
Blood gas lactate (mmol/L) (median [IQR])	1.6 [1.0, 2.1]
Leukocytes ($\times 10^9$ /L) (median [IQR])	9.5 [6.2, 13.2]
C-reactive protein (mg/L) (median [IQR])	100 [47, 208]
Scoring systems at ED triage	
qSOFA (median [IQR])	0 [0, 1]
SOFA (median [IQR])	3 [2, 4]
MEWS (median [IQR])	8 [6, 10]
Hemodynamic support therapy	
I.V. fluids in ED (3 h) (L) (median [IQR])	1 [0.5, 1.5]
Vasopressor therapy (i.e. noradrenaline) in ED (n(%))	1 (1)
Clinical deterioration outcomes	
Length-of-hospital stay (days) (median [IQR])	5.6 [3.2, 12.4]
SOFA rise ≥ 2 points (n(%))	8 (8)
Loop diuretics use <72 h (n(%))	12 (12)
Vasopressor therapy (i.e. noradrenaline) <72 h (n(%))	4 (4)
Mechanical ventilation (n(%))	3 (4)
CRRT <72 h (n(%))	0 (0)
ICU admission <72 h (n(%))	7 (7)
In-hospital mortality <72 h (n(%))	0 (0)
Mortality <30 days (n(%))	10 (10)

The table shows median and interquartile ranges (IQR) between brackets for continuous variables and absolute number and percentages for categorical variables. BMI: body mass index; CRRT: continuous renal replacement therapy; ICU: intensive care unit; IQR: Interquartile range; ED: emergency department; IV: intravenous; SOFA: Sequential Organ Failure Assessment; qSOFA: quick Sequential Organ Failure Assessment; MEWS: Modified Early Warning Score.

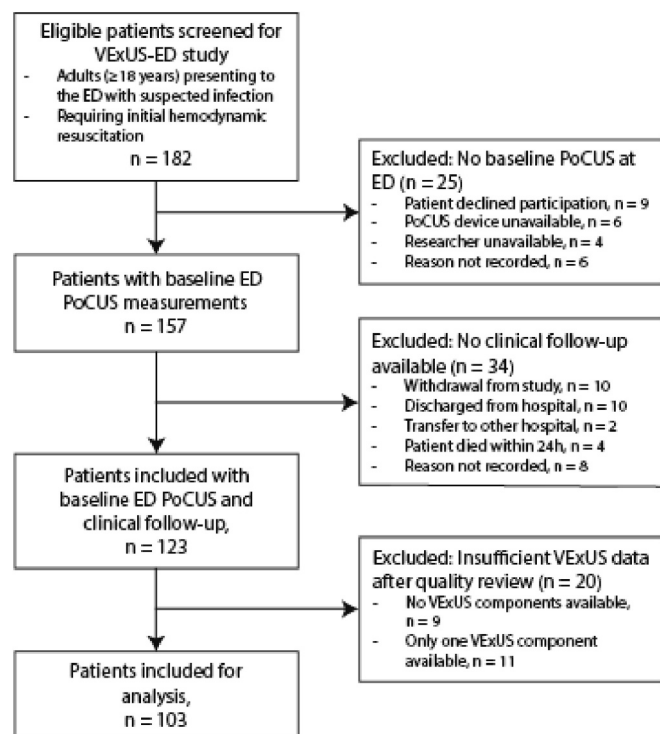


Fig. 2. Study flowchart of patient inclusion. Adult patients (≥ 18 years) presenting at the emergency department (ED) with suspected infection were screened for inclusion in the VExUS-ED study. Eligible patients required initial hemodynamic resuscitation, indicated by abnormal heart rate, blood pressure, shock index, or elevated blood lactate. Subsequently, patients were selected for analysis if point-of-care ultrasound (PoCUS) measurements were available both in the ED and at least one follow-up timepoint on day 1, day 2, or day 3. Patients were excluded from analysis if, after excluding poor-quality images, fewer than two VExUS components remained available for scoring. ED: emergency department; PoCUS: point-of-care ultrasound; VExUS: venous excess ultrasound;

Table 2

VExUS score and clinical parameters of each measurement.

	Measurement ED (n = 103)	Measurement Day 1 (n = 90)	Measurement Day 2 (n = 77)	Measurement Day 3 (n = 72)
VExUS grade (n(%))				
0	65 (75)	43 (57)	37 (54)	39 (62)
1	19 (22)	29 (38)	25 (37)	20 (32)
2	2 (2)	3 (4)	4 (6)	4 (6)
3	1 (1)	1 (1)	2 (3)	0 (0)
Missing	16	14	9	9
Inferior vena cava ≥2 cm (n(%))	22 (25)	33 (43)	31 (46)	24 (38)
Missing	16	14	9	9
Hepatic vein (n(%))				
S > D (normal)	73 (83)	67 (86)	59 (91)	58 (94)
D > S	7 (8)	5 (6)	2 (3)	2 (3)
S-wave reversal	8 (8)	6 (8)	4 (6)	2 (3)
Missing	15	12	12	10
Portal vein (n(%))				
No pulsatility (<30%) (normal)	68 (68)	67 (75)	55 (71)	59 (84)
Moderate pulsatility (30–49%)	25 (25)	20 (23)	19 (25)	9 (13)
Severe pulsatility (≥50%)	7 (7)	2 (2)	3 (4)	2 (3)
Missing	3	1	0	2
Intrarenal vein (n(%))				
Continuous flow (normal)	82 (87)	51 (67)	47 (61)	50 (75)
Discontinuous biphasic flow	12 (13)	23 (30)	15 (20)	15 (22)
Discontinuous monophasic flow	0 (0)	2 (3)	3 (4)	2 (3)
Missing	9	14	12	5
Clinical parameters				
MAP (mmHg) (median [IQR])	89 [79, 101]	83 [74, 92]	85 [75, 92]	87 [80, 97]
Heart rate (/min) (median [IQR])	110 [104, 122]	96 [83, 103]	90 [79, 98]	85 [78, 96]
Capillary refill time (s) (median [IQR])	3 [3, 4]	3 [2, 3]	3 [2, 3]	3 [2, 3]
MEWS (median [IQR])	8 [6, 10]	5 [4, 6]	4 [4, 6]	5 [4, 6]
Total amount of IV fluid administration (median [IQR])	1.0 [0.5, 1.5]	1.9 [1.3, 2.6]	3.5 [2.2, 5.0]	4.6 [3.1, 6.0]
Cumulative fluid balance (median [IQR])	0.9 [0.5, 1.5]	1.2 [0.3, 1.9]	1.8 [0.8, 2.9]	2.2 [0.6, 3.6]
Weight (kg) (median [IQR])	78 [63, 86]	76 [70, 88]	81 [72, 90]	81 [69, 90]

Daily overview of VExUS scores and individual components from Day 0 to Day 3 post-ED. Each column represents a specific day. The table shows the distribution of scores over time, with missing values indicated. Clinical parameters include key hemodynamic variables and relevant fluid-related measurements. Abbreviations: VExUS: venous excess ultrasound; IVC: inferior vena cava; MAP: mean arterial pressure; MEWS: modified early warning score.

within 72 h. Baseline VExUS scores were significantly higher in those who developed clinical fluid overload ($p = 0.002$). Moderate or severe congestion was observed in 15% with fluid overload versus none without, while mild congestion occurred in 26% versus 14%, respectively. Similarly, HV flow pattern abnormalities were more frequent in patients with fluid overload (30% vs 9%, $p = 0.021$), as were IRV flow pattern abnormalities (24% vs. 6%, $p = 0.018$). PV flow pattern abnormalities did not differ between groups ($p = 0.382$). An IVC diameter ≥ 2 cm was more common in patients with fluid overload (41% vs. 14%, $p = 0.006$), although 59% of fluid-overload patients had an IVC < 2 cm (Fig. 3). Baseline characteristics and clinical outcomes stratified by venous congestion (VExUS > 0 vs. 0) are shown in Supplementary Table 3 and Supplementary Fig. 1.

3.3. Association between VExUS scores and clinical fluid overload

In univariable logistic regression analyses, a baseline positive VExUS (VExUS > 0) score was associated with clinical fluid overload within 72 h (OR 4.13, 95% CI 1.61–11.04, $p = 0.004$), whereas IV fluid administration was not. After multivariable adjustment, a positive VExUS score remained associated with clinical fluid overload (aOR 3.83, 95% CI 1.34–11.58, $p = 0.014$) (Table 3). Among the individual components, abnormal HV flow patterns remained associated with fluid overload (aOR 4.20 (1.21–16.38), $p = 0.028$), whereas PV and IRV flow pattern were not associated (Table 3).

In longitudinal mixed-effects analysis incorporating VExUS measurements obtained at days 0–2, a positive VExUS score (VExUS > 0) was associated with next-day clinical fluid overload (OR 19.15, 95% CI 2.44–150.13, $p = 0.005$), whereas IV fluid administration was not. After adjustment, positive VExUS score remained associated with next-day

fluid overload (aOR 23.52, 95% CI 2.55–217.30, $p = 0.005$). Among the individual components, abnormal IRV flow pattern was independently associated with next-day fluid overload (aOR 11.63, 95% CI 2.00–67.66, $p = 0.006$), whereas HV and PV flow patterns were not associated (Table 3). These associations remained robust in best–worst case sensitivity analyses under extreme assumptions regarding missing congestion data (Supplementary Table 5).

Longitudinal VExUS trajectories are shown in Fig. 4, with component-level data presented in Supplementary Fig. 2. Transitions in VExUS status among patients with three consecutive measurements ($n = 54$) are shown in a complete-case alluvial plot (Supplementary Fig. 3).

3.4. Data quality assessment

Patients with excluded images more frequently had chronic heart failure, higher BMI, increased respiratory rate, and higher MEWS scores compared with patients with included images (Table 4). No differences were observed in MAP, heart rate, chronic kidney disease, liver disease, or history of transplantation. These exploratory comparisons were not adjusted for multiple testing and should be interpreted as hypothesis-generating.

Interrater agreement for ultrasound image interpretation across all measurement moments is presented in Table 5. Agreement was highest for IVC maximal diameter (87.4%, Cohen's $\kappa = 0.87$), followed by IRV flow patterns (85.6%, $\kappa = 0.61$). HV and PV flow patterns demonstrated moderate agreement (81.5%, $\kappa = 0.42$ and 73.4%, $\kappa = 0.48$, respectively).

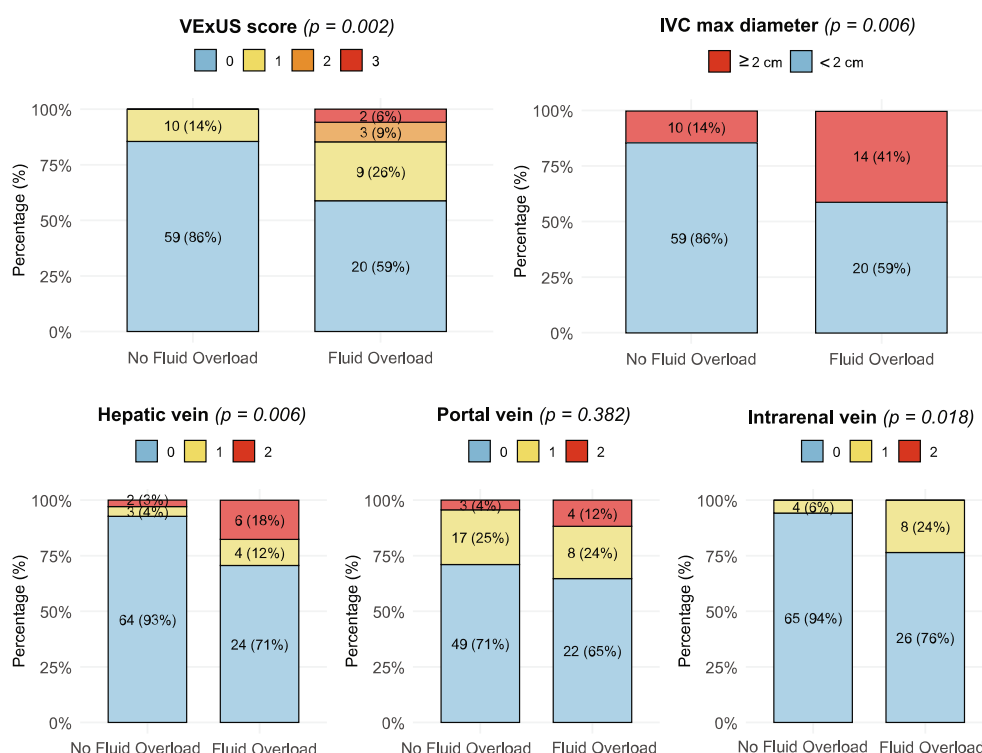


Fig. 3. Distribution of VExUS parameters measured at ED by clinical fluid overload status (<72 h) with corresponding p -values. Stacked bar plots show the distribution of the VExUS score, individual venous Doppler components (hepatic, portal, intrarenal), and IVC maximum diameter, stratified by clinical fluid overload (FO) status within 72 h of emergency department presentation: a composite outcome of a cumulative positive net fluid balance combined with at least one of the following: a 10% increase in body weight, the presence of bilateral B-lines on lung ultrasound or findings on chest X-ray consistent with pulmonary edema, or the use of loop diuretics. VExUS score categories differed significantly between groups ($p = 0.002$). Among the VExUS components, hepatic vein PWD patterns ($p = 0.006$) and intrarenal vein PWD patterns ($p = 0.018$) differed between patients who developed fluid overload and those who did not. An IVC diameter ≥ 2 cm occurred more frequently in patients with fluid overload ($p = 0.006$). Data are presented as number (percentage) of patients per group. Statistical comparisons were performed using Fisher's exact test. HV: hepatic vein; IRV: intrarenal vein; IVC: inferior vena cava; PV: portal vein; VExUS: venous excess ultrasound;

4. Discussion

In this study, we evaluated the venous excess ultrasound (VExUS) in the ED and early post-ED period among patients with suspected sepsis receiving IV fluids. Moderate to severe venous congestion (VExUS ≥ 2) was uncommon at baseline. However, higher VExUS grades and abnormal hepatic and intrarenal vein patterns were more frequent among patients who developed fluid overload, whereas portal vein patterns did not differ. Even mild elevations in VExUS scores were associated with subsequent fluid overload, independent of the volume of IV fluids administered, supporting the concept that fluid overload in sepsis reflects impaired fluid tolerance rather than absolute fluid volume (24). Collectively, these findings suggest that VExUS may help identify patients approaching their fluid tolerance limit and at risk of fluid overload before severe organ dysfunction occurs.

Venous congestion assessment based on Doppler flow patterns may provide clinically relevant information in this setting. IVC assessment is commonly used but is known to be challenging and sometimes unreliable in the ED, leading to missing or inconclusive measurements (25–29). Fixed IVC thresholds do not account for inter-individual variability (30), and sepsis-related hemodynamic changes may produce congestion patterns distinct from heart failure (31–33). In our cohort, 59% of patients who developed fluid overload had an IVC <2 cm, suggesting that reliance on an IVC size threshold alone may miss relevant congestion. Abnormal hepatic vein and intrarenal vein Doppler patterns were associated with clinical fluid overload, supporting the potential role of venous Doppler assessment as an alternative to IVC-based VExUS assessment in the ED, although further studies are needed to validate this approach.

Venous congestion may develop despite a normal baseline VExUS,

highlighting the importance of repeated assessment. In our cohort, some patients who developed fluid overload initially had a VExUS of 0 and received additional IV fluids during ongoing resuscitation and maintenance therapy (34–36). This dynamic interplay between fluid administration and evolving congestion supports the use of serial VExUS measurements, integrated with conventional hemodynamic and fluid balance parameters, to detect developing fluid intolerance and guide decisions on whether to continue, reduce, or stop IV fluids during ongoing sepsis resuscitation (37–39).

Although the study cohort consisted mainly of hemodynamically stable patients with mild tachycardia and low lactate levels, one-third developed clinical fluid overload within 72 h while receiving standard IV fluid therapy (40,41). This suggests that fluid administration driven by tachycardia alone, which may reflect systemic inflammation rather than hypovolemia, risks unnecessary fluid loading (42,43). Excessive fluid accumulation in sepsis is associated with organ dysfunction and worse outcomes (44,45), emphasizing the need for careful fluid stewardship potentially supported by early, noninvasive congestion markers such as VExUS.

Our findings should be interpreted in the context of an emergency department population with predominantly mild-to-moderate sepsis, presenting early in the disease course with mild tachycardia and low lactate levels, prior to progression to established septic shock. As such, these results may not be directly generalizable to ICU cohorts, where congestion severity, monitoring intensity, and VExUS trajectories differ. In ICU settings, higher and more persistent VExUS scores are commonly reported, with limited temporal variation, likely reflecting greater illness severity as well as closer hemodynamic monitoring and more frequent fluid titration (19,46). In contrast, patients in ward settings often receive ongoing IV fluids with less intensive monitoring, allowing

Table 3
Logistic and longitudinal mixed-effects regression analyses of VExUS and clinical fluid overload.

	Simple logistic regression analysis				Mixed-effects logistic regression analysis			
	Univariable		Multivariable		Univariable		Multivariable	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
VExUS scoring systems at ED								
VExUS score								
VExUS ≥ 0 (any congestion)*	4.13 (1.61–11.04)	0.004	4.46 (1.71–12.20)	0.003	3.83 (1.34–11.58)	0.014	19.15 (2.44–150.13)	0.005
IV fluid administration	1.24 (0.78–1.97)	0.353	1.35 (0.83–2.20)	0.210	1.18 (0.71–2.00)	0.585	0.86 (0.58–1.29)	0.469
VExUS components								
Hepatic vein: abnormal flow pattern	5.33 (1.71–18.65)	0.005	5.66 (1.80–20.12)	0.004	4.20 (1.21–16.38)	0.028	15.52 (1.03–233.65)	0.048
Portal vein: abnormal flow pattern	1.34 (0.55–3.19)	0.516	1.35 (0.55–3.25)	0.501	1.27 (0.48–3.31)	0.618	1.45 (0.31–6.80)	0.636
Intrarenal vein: abnormal flow pattern	5.00 (1.45–20.09)	0.014	4.85 (1.39–19.57)	0.016	3.30 (0.89–13.92)	0.081	11.18 (1.16–11.20)	<0.001

Baseline (day 0) and longitudinal (days 0–2) VExUS status (VExUS >0) and individual VExUS components (hepatic vein, portal vein, intrarenal vein) were evaluated for their association with clinical fluid overload within 72 h and on the subsequent day, respectively. *An inferior vena cava (IVC) diameter ≥ 2 cm was considered equivalent to VExUS >0. Clinical fluid overload was defined as a net positive cumulative fluid balance combined with ≥10% body weight increase, pulmonary edema on lung ultrasound or chest X-ray, or use of loop diuretics. Baseline associations were assessed using logistic regression, and longitudinal associations using mixed-effects logistic regression with patient ID as a random effect. Results are presented as odds ratios (ORs) with 95% confidence intervals (CIs) and p-values. Univariable, multivariable (adjusted for IV fluid administration), and fully adjusted models (additional adjustment for age, sex, and Charlson Comorbidity Index) are shown. Statistically significant results are indicated in bold. CI: confidence interval; IV: intravenous; IVC: inferior vena cava; OR: odds ratio; VExUS: venous excess ultrasound.

venous congestion to develop without early recognition (47,48). These differences emphasize the importance of interpreting VExUS within its clinical context and support the use of serial assessments to detect early venous congestion, particularly outside the ICU.

4.1. Clinical relevance

Early identification of venous congestion using VExUS provides a rapid, noninvasive bedside approach to recognize patients at risk of developing clinical fluid overload. Integrating VExUS into sepsis care may support more individualized fluid management by balancing adequate perfusion against the risk of congestion, including in patients who appear fluid responsive but are close to their fluid tolerance limit (11). Simplified approaches focusing on selected venous Doppler signals, such as hepatic or intrarenal venous flow (49,50), may improve feasibility in acute care settings and can be complemented by other ultrasound modalities, including lung ultrasound and Doppler-derived LVOT velocity time integral (VTI) measurements, to further support fluid stewardship (51,52).

4.2. Strengths and limitations

This study is the first to evaluate repeated VExUS assessments in an ED sepsis population, providing insight into early and dynamic changes in venous congestion over the first 72 h after presentation. Ultrasound examinations were generally feasible when performed by operators with limited training, supporting the applicability of VExUS in real-world ED settings (53,54). Despite a predominantly mild-to-moderate ED sepsis cohort, one-third of patients developed clinical fluid overload, underscoring the clinical relevance of early congestion detection and individualized fluid strategies.

This study has limitations. Its single-center design and modest sample size may limit generalizability, and moderate-to-severe VExUS grades were uncommon, restricting assessment of higher-grade congestion. Image acquisition was more challenging in patients with higher BMI, greater illness severity, or chronic heart failure, potentially limiting applicability in those at highest risk (53). These challenges, along with the requirement for serial VExUS assessments, may have introduced survivorship and selection bias through underrepresentation of patients with early mortality or technically limited imaging, potentially influencing the observed associations. However, best-worst case sensitivity analyses supported robustness of the primary findings. While clinical fluid overload and venous congestion represent related but distinct physiological constructs, low event rates for alternative outcomes such as organ dysfunction or mortality justified this pragmatic outcome choice in this exploratory study. Interobserver agreement varied across venous Doppler components, potentially reflecting technical and interpretative complexity, thereby emphasizing the importance of standardized training, ECG enhancement, and careful image acquisition for reliable clinical use (55,56).

4.3. Future implications

Future studies should evaluate how VExUS can be integrated into early sepsis resuscitation to guide real-time fluid therapy. Serial VExUS assessments may help identify patients approaching their fluid tolerance limit and support tailored fluid strategies (57). Several ICU-based studies, including the ANDROMEDA-2 VExUS study (58), and the upcoming VESPER trial (NCT06696391), are evaluating VExUS-guided fluid management. Given that initial fluid resuscitation often occurs before ICU admission, complementary studies in earlier phases of care, such as in the emergency department and hospital ward (e.g. FLUIDS trial), are needed to define the role of VExUS across the continuum of acute care (59). Evaluation of modified approaches and their integration with dynamic measures of fluid responsiveness remains an important area for future research (60).

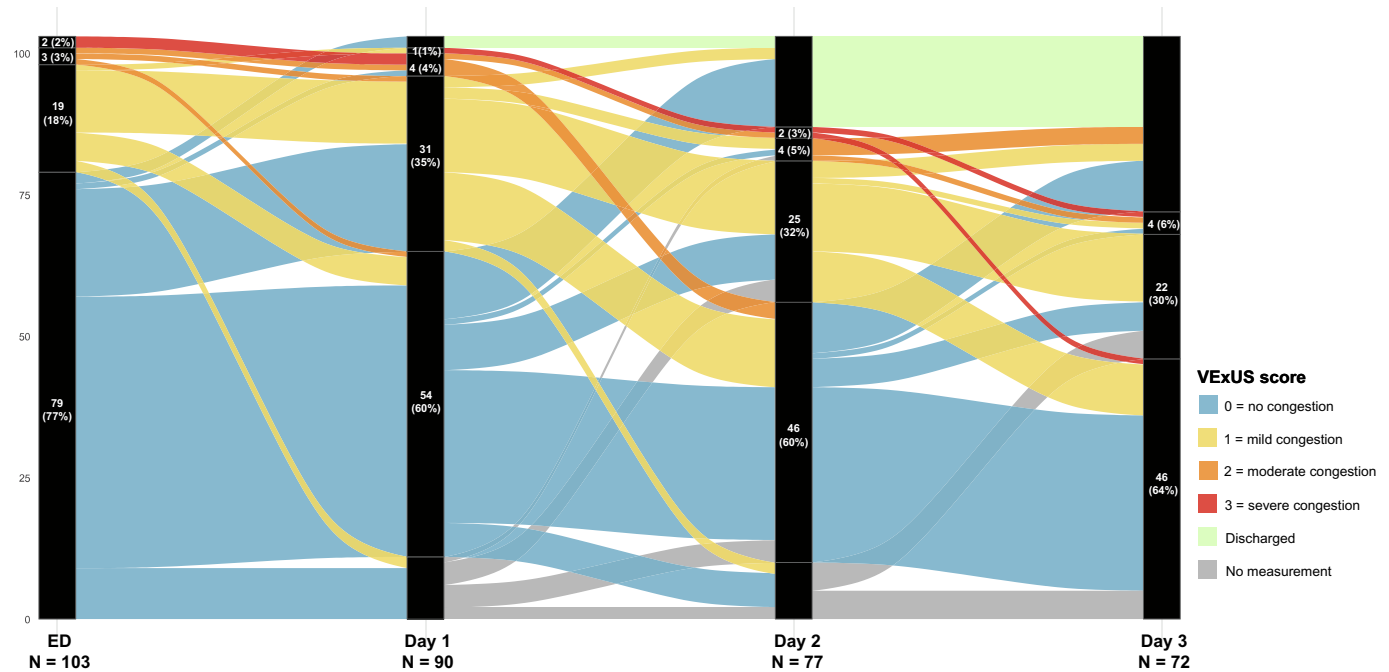


Fig. 4. Alluvial representation of VExUS score trajectories from day 0 to day 3 The alluvial plot illustrates VExUS score trajectories over the first 72 h. Each flow represents an individual patient, connecting daily scores across day 0 to day 3. The color of each flow segment corresponds to the VExUS score at the start of that segment, whereas the vertical position reflects the actual score each day.

Table 4
Potential factors associated with excluded imaging data.

	Included (n = 103)	Excluded (n = 20)	p-value
Demographics			
Female (n (%))	49 (48%)	8 (40%)	0.707
Age (median [IQR])	64 [51, 72]	69 [65, 72]	0.079
BMI (median [IQR])	25.3 [22.5, 28.4]	27.8 [25.7, 32.8]	0.015
Vital parameters at triage			
Mean arterial pressure [mmHg] (median [IQR])	89 [79, 101]	90 [84, 103]	0.696
Heart rate [/min] (median [IQR])	110 [104, 122]	116 [106, 139]	0.096
Respiratory frequency [/min] (median [IQR])	20 [16, 24]	23 [21, 26]	0.042
MEWS score (median [IQR])	5 [3, 7]	8 [5, 10]	0.002
Comorbidities			
Chronic heart failure (n (%))	5 (5%)	5 (25%)	0.010
Chronic kidney disease (n (%))	19 (18%)	6 (30%)	0.235
Chronic liver disease (n (%))	5 (5%)	3 (15%)	0.384
Transplantation (n (%))	21 (20%)	3 (15%)	0.804

The table presents patient characteristics stratified by image inclusion status (included, n = 103; excluded, n = 20). Continuous variables are summarized as median (interquartile range) and categorical variables as counts (percentages). Comparisons show that patients with excluded images had higher BMI ($p = 0.015$), increased respiratory rate ($p = 0.042$), and higher MEWS scores ($p = 0.002$), while no differences were observed in MAP, heart rate, chronic kidney disease, liver disease, or history of transplantation. Statistical tests were performed using the Mann–Whitney U test for continuous variables and Chi-square or Fisher's exact test for categorical variables. Significant p -values are highlighted in bold. BMI: body mass index; MEWS: modified early warning score; IQR: interquartile range;

5. Conclusion

In patients with suspected sepsis, even mild early venous congestion (VExUS >0) was independently associated with clinical fluid overload within 72 h. Abnormal hepatic and intrarenal flow patterns may provide

Table 5
Interrater agreement between the first and second reviewer for ultrasound image interpretation across all measurement moments (D0–D3).

	% of agreement	Cohens' kappa
Ultrasound image		
Inferior vena cava (max diameter)	87.4%	0.87
Hepatic vein (PWD pattern)	81.5%	0.42
Portal vein (PWD pattern)	73.4%	0.48
Intrarenal vein (PWD pattern)	85.6%	0.61

This table shows the overall percentage of agreement and Cohen's kappa coefficients for each ultrasound component of the VExUS score. Agreement was calculated across all available images from day 0 to day 3. Agreement for IVC diameter was strong (87.4%, $\kappa = 0.87$). Hepatic and portal vein patterns showed moderate agreement (81.5%, $\kappa = 0.42$ and 73.4%, $\kappa = 0.48$, respectively), whereas intrarenal vein patterns demonstrated substantial agreement (85.6%, $\kappa = 0.61$). PWD: pulse wave doppler;

additional information on venous congestion beyond the original VExUS score. Early and serial VExUS assessments may offer a rapid and noninvasive means to identify limited fluid tolerance and support individualized fluid management in sepsis.

CRediT authorship contribution statement

Sanne Ter Horst: Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jochem van Oosten:** Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Ranek Laros:** Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Bashar Sukkar:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Jildou van Everdink:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Alessandra di Mauro:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Adyaan Alawi:** Writing – review & editing, Resources, Data curation. **Willemijn de Vries:** Writing – review & editing, Resources, Data curation. **Michèle ter Voert:** Writing – review & editing, Resources,

Data curation. **Ilektra Koliaki**: Writing – review & editing, Resources, Data curation. **Amber Slot**: Writing – review & editing, Resources, Data curation. **Donna van der Wiel**: Writing – review & editing, Resources, Data curation. **Jingyi Lu**: Writing – review & editing, Resources, Data curation. **Lucia Colavolpe**: Writing – review & editing, Resources, Data curation. **Deborah Blanca**: Writing – review & editing, Methodology, Data curation, Conceptualization. **Hjalmar R. Bouma**: Writing – review & editing, Supervision, Methodology, Conceptualization. **Jan C. ter Maaten**: Writing – review & editing, Supervision, Methodology, Data curation, Conceptualization. **Tycho J. Olgers**: Writing – review & editing, Validation, Supervision, Project administration, Methodology, Data curation, Conceptualization.

Ethics approval and consent to participate

Acutelines is approved by the medical ethics board of the UMCG and registered under trial registration number NCT04615065 at [ClinicalTrials.gov](https://clinicaltrials.gov). The study protocol was approved by the institutional review board (IRB) under registration number 21256. A deferred consent procedure (by proxy) was in place to enable the collection of data and biomaterials before obtaining written consent.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcrr.2026.155488>.

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