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Upper Limb Edema as Predictor of Difficult Peripheral Intravenous Cannulation

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ABSTRACT

Background: Predictors of difficult peripheral intravenous cannulation include nonvisible and non-palpable veins, history of difficult access, intravenous drug use, abnormal body mass index, vascular disease, and conditions such as wasting syndrome, diabetes, sickle cell disease, hemodialysis, chronic obstructive pulmonary disease, and upper limb alterations, including edema. This study evaluated the predictive accuracy of upper-limb edema in identifying difficult intravenous catheter placement. **Methods:** A secondary analysis was conducted on data from a large prospective observational study investigating the prevalence of difficult intravenous access (DIVA), cannulation timing, and enhanced adult-DIVA (EA-DIVA) thresholds for ultrasound guidance at the emergency department of an urban general hospital. Logistic regression was used to identify predictors of ultrasound-guided cannulation. **Results:** Significant predictors of DIVA included overweight (odds ratio [OR] = 3.934; 95% CI: 2.218-6.977), neurovascular diseases (OR = 3.106; 95% CI: 1.650-5.845), and upper-limb edema (OR = 3.026; 95% CI: 1.542-5.937). Other predictors were history of difficult cannulation (OR = 2.675), vascular depletion (OR = 2.669), abnormal vein evaluation (OR = 2.649), and abnormal skin assessment (OR = 1.841). **Conclusion:** Upper-limb edema emerged as a strong, independent predictor of DIVA not currently included in the EA-DIVA score. Its immediate clinical detectability suggests its potential as a binary screening criterion for direct referral to ultrasound-guided cannulation.

Key words: difficult access, difficult intravenous access, DIVA, emergency department, limb edema, ultrasound, ultrasound-guided, vein cannulation

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INTRODUCTION

Approximately 70% to 80% of hospitalized patients require the insertion of a short peripheral catheter (SPC),¹ and among these, over 59.3% are classified as having difficult intravenous access (DIVA).² In this population, the SPC insertion failure rate ranges between 35% and 50%, even when performed by skilled health care professionals.^{1,3} This high failure rate contributes to the progressive deterioration of venous access, a phenomenon referred to as “vascular exhaustion,” which increasingly complicates future peripheral cannulation attempts.⁴ The most commonly used criterion for identifying patients with DIVA is failure of 2 or more attempts to secure peripheral intravenous access.^{5,6} In terms of clinical outcomes, patients with DIVA experience a higher incidence and severity of complications related to SPCs, such as infections and thrombosis, which in turn, are associated with a prolonged hospital stay and increased health care costs.⁴

Several factors have been identified as significant predictors for difficult peripheral intravenous cannulation. These include nonvisible and nonpalpable veins on physical examination, a history of DIVA (reported in the clinical record or by the patient),⁴ the use of venipuncture-assisting technologies,⁷ intravenous drug use, body mass index (BMI) > 25^{8,9} or under 18.5,¹⁰ vascular disease,¹¹ and other conditions such as cachexia (wasting syndrome), diabetes mellitus, sickle cell disease,¹² hemodialysis, chronic obstructive pulmonary disease, and upper limb alterations, including edema, hematoma, inflammation, or previous surgeries.⁴ The success of cannulation is also influenced by the health care provider’s level of experience and specific skills in peripheral access placement, which can significantly affect procedural outcomes.¹³ Furthermore, difficulty in obtaining peripheral access is associated with increased use of central vascular access devices (CVADs), often not due to therapeutic necessity but rather as a consequence of failed peripheral attempts.¹⁴

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In this context, early identification of patients at risk of DIVA is critical. The enhanced adult-DIVA (EA-DIVA) score has emerged as a reliable tool for this purpose.¹⁵ This score incorporates 8 variables known to influence cannulation difficulty: history of difficult peripheral access; vascular depletion; coagulation disorders and/or use of anticoagulant or antiplatelet medications; neurovascular disease; abnormal skin characteristics (eg, dark, thick, or fragile skin); overweight status; vein characteristics (nonvisible, nonpalpable, tortuous, or winding); and unilateral vein availability. The score ranges from 0 to 12, with a cutoff of ≥ 8 , indicating the need for advanced techniques or specialist interventions for SPC placement.

A recent study performed in the emergency department (ED) suggested that a lower EA-DIVA cutoff score of 6 may offer greater sensitivity and specificity for identifying patients with difficult intravenous cannulation.¹⁶ However, despite the high accuracy of the tool, certain variables may still be overlooked in clinical practice. In particular, edema can significantly impair vein visibility and palpability, further complicating SPC placement.¹⁷ During data analysis, a substantial proportion of patients presented with upper limb edema.¹⁶ As this variable is not currently included in the EA-DIVA score, this study aimed to investigate whether the presence of edema may serve as an independent predictive factor for DIVA in ED patients and whether it should be considered for inclusion in a comprehensive venous access assessment alongside the EA-DIVA score.

Objectives

This study aimed to evaluate the predictive accuracy of upper limb edema in identifying difficulties in peripheral intravenous catheter placement, specifically in terms of the number of insertion attempts and time required to complete the procedure.

METHODS

Study Design, Setting, and Sampling

This is a secondary analysis of the results from a large prospective observational study conducted between January and October 2024. The study aimed to determine the prevalence of DIVA, assess intravenous cannulation timing, and identify EA-DIVA score thresholds for the call of ultrasound guidance for peripheral intravenous catheter placement at the ED of San Giuseppe Hospital, Empoli (Florence, Italy). Adult patients ($n = 1280$) were recruited from the ED and evaluated by emergency nurses ($n = 23$) with 1 to 25 years of experience. The study protocol was approved by the local ethics committee (protocol number 24028_oss) and adhered to the principles outlined in the Declaration of Helsinki and Good Clinical Practice. Further methodological details, including patient selection and primary findings, have been previously reported.¹⁶

Data Sources and Data Collection

Demographic and medical history data were extracted from the electronic health records, whereas other variables were collected using a standardized Case Report Form. The study collected demographic and clinical data of patients (eg, blood pressure, body temperature, medical and vascular), as well as history and details of SPC placement (eg, the health care professional performing the procedure, device type and gauge, insertion site, number of attempts, and time taken for insertion) and technique used (standard or ultrasound-guided). Procedural complications, such as nerve or arterial puncture, bruising, extravasation, and hematoma, were also recorded. Short peripheral catheter placement was initiated by nurses using a conventional technique upon patient admission, with the equipment prepared according to standard procedures. The insertion time was recorded, and successful placement was confirmed by the absence of extravasation or occlusion following a saline flush. Ultrasound guidance was used in patients with DIVA. If multiple SPC attempts failed, alternative devices, including long peripheral catheters and CVADs were used. Ultrasound guidance was used to optimize the accuracy of catheter placement and minimize insertion failure. All procedures were performed using wall clocks available in the ED.

Statistical Analysis

Data were analyzed using descriptive statistics (central tendency and dispersion) appropriate for variable distributions. Associations between the variables of interest were investigated using regression models based on variable type. First, both the contribution of EA-DIVA items and clinical factors to the number of venipuncture attempts was assessed using linear regression models. Next, the ability of EA-DIVA items, together with the presence of edema, to predict ultrasound use was evaluated using logistic regression models. In both cases, univariate models were first used to identify variables for inclusion in the multivariate models; the *P*-value threshold adopted at this stage was *P* < .10. The identified variables were then entered into multivariate models using a stepwise backward elimination approach, adopting a statistical significance threshold of *P* < .05. Statistical analyses were performed using IBM SPSS 22, STATA 16, and GraphPad Prism 6.

RESULTS

Characteristics of the Participants

Patients (n = 1280) were typically older adults (median age: 70 years; interquartile range [IQR] 50-82), predominantly female (n = 655; 51.17%), and White (n = 1133; 88.52%).¹⁶ Upper limb edema was observed in 6.72% (n = 86) of patients, of whom 34.15% (n = 28) had unilateral edema and 65.85% (n = 54) had bilateral edema (unspecified side in 4 cases). When present, edema was typically pitting in nature and associated with vascular fragility, potentially

contributing to DIVA. Table 1 summarizes the clinical characteristics of the participants.

Predictive Analysis of EA-DIVA Variables on the Number of Venipuncture Attempts

Multiple linear regression analysis was performed to assess the predictive contribution of each EA-DIVA item to the total number of venipuncture attempts (Table 2). All predictors were statistically significant (*P* ≤ .0001). The strongest associations were found for vascular depletion due to intravenous drug use (β = 1.9436) and previous venipuncture (β = 1.5154). Additional relevant predictors included chemotherapy-related depletion (β = 0.8103), one-side-only vein availability (β = 0.7604), and neurovascular disease (β = 0.7002). Site-related variables were also significant: non-visible/rolling veins (β = 0.5497), altered skin assessment (β = 0.5009), and being overweight (BMI > 25) (β = 0.6071). Minor but significant effects were observed for coagulopathy/anticoagulant use (β = 0.2193) and history of difficult access (β = 0.4440).

Predictive Analysis of Non-EA-DIVA Variables on the Number of Venipuncture Attempts

Multiple linear regression was conducted on clinical and anamnestic variables that showed significant associations with the number of venipuncture attempts in the bivariate

TABLE 1

Clinical Characteristics of the Participants (N = 1280)

Remote Pathological History	n (%)
Circulatory system disease	552 (43.13)
Coagulative disorder and/or intake of anticoagulant or antiplatelet drugs	419 (32.73)
Overweight ^a	344 (26.90)
Diabetes mellitus	259 (20.23)
Endocrine, nutritional, and metabolic disease	226 (17.68)
Nervous system disease	153 (11.96)
Oncological disease	129 (10.08)
Previous use of chemotherapeutic agents	120 (9.38)
Respiratory system disease	107 (8.36)
Chronic kidney disease	79 (6.17)
Digestive system disease	73 (5.70)
Other disease/conditions	57 (4.45)
Disease of the genitourinary system	43 (3.36)
Rheumatic diseases	18 (1.41)
Sickle cell anemia	16 (1.25)
Previous use of intravenous drug abuse	10 (0.78)

^aOverweight: Body Mass Index > 25.

analysis to assess their independent predictive value, while accounting for potential confounders (Table 3). Upper limb edema emerged as the strongest predictor ($\beta = 1.3780$), followed by oncological diseases ($\beta = 0.6229$), respiratory diseases ($\beta = 0.5829$), endocrine-metabolic disorders ($\beta = 0.5311$), neurological conditions ($\beta = 0.4322$), and cardiovascular diseases ($\beta = 0.3840$). Other significant predictors included diabetes mellitus ($\beta = 0.3484$) and other chronic conditions ($\beta = 0.4808$). Systolic blood pressure showed a small but significant inverse association with the number of attempts ($\beta = -0.004$; $P = .007$). The remaining variables, including smoking history, body temperature, and various comorbidities, did not reach statistical significance in the multivariate model.

Predictors of Ultrasound-Guided Cannulation

To investigate the factors associated with the use of ultrasound-guided techniques for peripheral intravenous cannulation, logistic regression analysis was performed (Table 4). Together with obesity (BMI >25; odds ratio [OR] = 3.934) and neurovascular diseases (OR = 3.106), upper limb edema was one of the most influential predictors (OR = 3.026), confirming its impact on venous access complexity. Other significant predictors included history of DIVA (OR = 2.675), vascular depletion (OR = 2.669), abnormal skin assessment (OR = 1.841), and abnormal vein evaluation (OR = 2.649). Figure 1 presents a proposed decision-making algorithm for the management of peripheral intravenous catheters (PIVCs) in ED patients, incorporating the observation of edema and the newly suggested EA-DIVA 6 cutoff.

DISCUSSION

The aim of this study was to assess the predictive value of upper limb edema in determining peripheral intravenous

cannulation difficulty, as measured by the number of attempts and duration of the procedure, in a large inpatient hospital cohort. The results demonstrated that upper limb edema was a strong independent predictor of multiple venipuncture attempts and significantly associated with the use of ultrasound-guided cannulation.

Additional clinical and anamnestic factors, such as oncological, respiratory, and endocrine-metabolic conditions, also showed significant associations with increased procedural complexity, in line with previous studies reported in the literature.^{4,8,10,11} The predictive validity of the EA-DIVA score was confirmed within the clinical context.

To date, the role of edema in peripheral venous access has received limited attention. According to current knowledge, this is the first study to quantify the predictive value of upper limb edema using multivariate analysis in a large, hospitalized population. Among the conditions identified, upper limb edema is unique in that it can be immediately assessed during clinical examination without requiring prior patient history, thus making it especially relevant in time-sensitive environments such as the ED.

Patients with upper limb edema required significantly more insertion attempts than those without. This not only impacts patient comfort and satisfaction but also increases the risk of complications such as phlebitis or hematoma. Despite the existing literature discussing various anatomical and clinical predictors of DIVA, no prior studies have directly quantified the impact of edema on cannulation attempts, making this a novel contribution.

Moreover, it can be hypothesized that the presence of edema is associated with prolonged cannulation time, likely due to impaired vein visibility and palpability. Although studies have previously highlighted time as an outcome variable in relation to device or operator skill,

TABLE 2
Influence of EA-DIVA Items on the Total Number of Venipuncture Attempts

EA-DIVA Score Items	Coeff. B	SE	95% CI	P Value
History of difficult intravenous access	0.4440	0.1557	0.413-0.474	≤.0001
Vascular depletion due to previous use of chemotherapeutic agents	0.8103	0.0849	0.644-0.9796	≤.0001
Vascular depletion due to previous use of intravenous drug abuse	1.9436	0.2803	1.394-2.493	≤.0001
Vascular depletion due to previous venipunctures	1.5154	0.1035	1.312-1.718	≤.0001
Coagulative disorder and/or intake of anticoagulant or antiplatelet drugs	0.2193	0.0585	0.104-0.334	≤.0001
Neurovascular disease	0.7002	0.0825	0.538-0.862	≤.0001
Clinical examination of skin	0.5009	0.0556	0.392-0.610	≤.0001
Overweight ^a	0.6071	0.0599	0.490-0.725	≤.0001
Vein evaluation: not visible, not palpable, rolling or winding vein	0.5497	0.0233	0.504-0.595	≤.0001
One-side only availability	0.7604	0.1754	0.416-1.105	≤.0001

Abbreviations: CI, confidence interval; Coeff. B, Beta coefficient; EA-DIVA, enhanced adult-difficult intravenous access; SE, standard error.
^aOverweight: Body Mass Index > 25.

TABLE 3

Influence of Non-EA-DIVA Items on the Total Number of Venipuncture Attempts

Item	Coeff. β	SE	95% CI	P Value
Oncological diseases	0.6229	0.0899	0.446 to 0.799	<.0001
Diabetes mellitus	0.3484	0.0679	0.215 to 0.482	<.0001
Upper limb edema	1.3780	0.1032	1.175 to 1.580	<.0001
Cardiovascular diseases	0.3840	0.0546	0.277 to 0.491	<.0001
Neurological conditions	0.4322	0.0842	0.267 to 0.597	<.0001
Endocrine-metabolic disorders	0.5311	0.0708	0.392 to 0.670	<.0001
Respiratory diseases	0.5829	0.0983	0.390 to 0.776	<.0001
Other conditions	0.4808	0.1330	0.220 to 0.742	<.0001
SBP	-0.004	0.0013	-0.006 to 0.001	.007
Smoke ^a	0.1425	0.0932	-0.040 to 0.325	.127
Body temperature	0.5255	0.4177	-0.029 to 0.134	.209
Smoking history	0.0876	0.0736	-0.232 to 0.569	.235
Gastrointestinal diseases	0.1385	0.1188	-0.095 to 0.372	.244
Rheumatic diseases	-0.1539	0.2341	-0.613 to 0.305	.511
Sickle cell anemia	0.0854	0.2481	-0.401 to 0.572	.731
Urological diseases	0.0417	0.1530	-0.258 to 0.342	.785
Chronic renal failure	0.0309	0.1145	0.194 to 0.255	.787

Abbreviations: CI, confidence interval; Coeff. β , Beta coefficient; SBP, systolic blood pressure; SE, standard error.

^aSmoke: Current smoking status.

very few have investigated its association with specific physical findings, such as edema. This finding underlines the potential of edema as a rapid and objective marker for anticipating procedural delays and accordingly allocating advanced techniques (eg, ultrasound guidance). Indeed, the accumulation of fluid in the tissues caused by edema can alter the visibility and palpability of superficial veins¹⁷

and can change the consistency and the response of the vein to tourniquet pressure, making the placement of a peripheral venous access device more difficult, with a resulting increase in the likelihood of failure on the first attempt and the need for multiple attempts.

The consequences for the patient may include delays in clinical management, increased risk of adverse events,

TABLE 4

Logistic Regression Analysis of Risk Factors for the Use of Ultrasound-Guided Peripheral Intravenous Cannulation

Risk Factor	OR	SE	95% CI	P Value
Upper limb edema	3.026	1.041	1.542-5.937	.001
History of difficult peripheral intravenous cannulation	2.675	0.451	1.922-3.722	≤.001
Vascular depletion	2.669	0.371	2.032-3.505	≤.001
Neurovascular disease	3.106	1.002	1.650-5.845	≤.001
Clinical examination of skin	1.841	0.532	1.045-3.241	.035
Overweight ^a	3.934	1.150	2.218-6.977	≤.001
Vein evaluation: not visible, not palpable, rolling or winding vein	2.649	0.841	1.422-4.937	.002

Abbreviations: CI, confidence interval; OR, odds ratio; SE, standard error.

^aOverweight: Body Mass Index > 25.

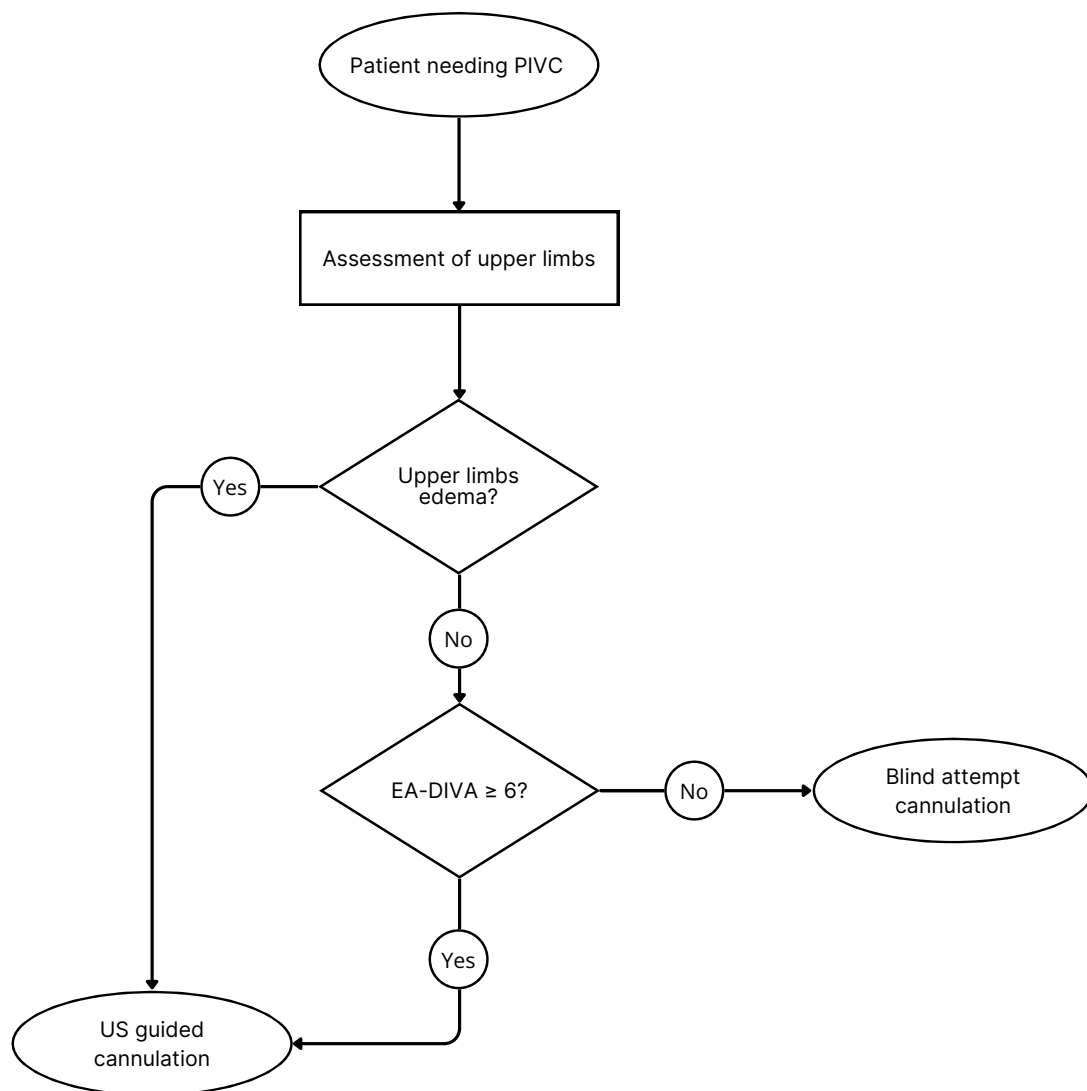


Figure 1. Proposal of decisional flowchart for the management of peripheral intravenous catheters in the emergency department. *Abbreviations:* EA-DIVA, enhanced adult-difficult intravenous access; PIVC, peripheral intravenous catheter; US, ultrasound. Note: The proposed flowchart is to be interpreted with caution and requires further validation through methodologically robust studies.

higher hospitalization costs, stress for both the patient and the caregiver, pain, anxiety and discomfort, and infections or phlebitis related to repeated venipuncture attempts.^{3,18,19}

Therefore, upper limb edema could serve as a useful indicator of potential difficulty in placing an SPC. Including edema in the assessment of peripheral intravenous access could allow for a more targeted and reliable management, improving the effectiveness of procedures and reducing risks for the patient.

Beyond its predictive value, the prevalence and immediate detectability of upper limb edema warrant further consideration. In the present study, this condition was frequently observed at the bedside, emphasizing the need to recognize its potential impact on vascular access, particularly in urgent clinical contexts.

A key concern relates to the inherently subjective nature of edema assessment. Unlike most components of

the EA-DIVA score, which are based on objective criteria, edema is evaluated through visual inspection and manual palpation, introducing potential interoperator variability. However, other elements of the score, such as vein palpability and fragility, also rely on clinical judgment, indicating that with appropriate standardization, edema can be incorporated without compromising scoring reliability. In the present study, edema was not systematically categorized but was documented as a clearly visible clinical sign, detectable at the patient's bedside without requiring a review of medical history or additional questioning. Its predictive value emerged post hoc from the analysis, demonstrating a strong association with both the number of cannulation attempts and the likelihood of requiring ultrasound-guided access. These findings suggest that even basic visual identification of edema carries significant predictive weight. Future research should aim to develop standardized

assessment criteria for edema, incorporating dimensions, such as extent, depth, and type (eg, pitting), to enable more accurate stratification of DIVA and inform early decisions regarding ultrasound use. This finding supports the consideration of upper limb edema, particularly pitting edema, as a warning sign for DIVA, to inform early clinical decision-making. Nevertheless, nurses are encouraged to integrate this information with critical thinking and clinical intuition when assessing patients for PIVC placement. Such developments may improve existing triage algorithms or contribute to the refinement of tools based on the EA-DIVA framework.

STRENGTHS AND LIMITATIONS

This study has several strengths. First, it provides novel evidence regarding the predictive role of upper limb edema in peripheral intravenous cannulation outcomes, based on a large, well-characterized inpatient sample from an ED setting. The prospective design and rigorous data collection procedures, involving experienced emergency nurses, enhance the internal validity of the findings. Furthermore, the multivariate analysis enabled adjustment for multiple clinical and demographic covariates, allowing for the identification of edema as an independent predictor of DIVA. The integration of both EA-DIVA and non-EA-DIVA variables offers a comprehensive overview of the multifactorial nature of DIVA, reinforcing the potential utility of expanding the current scoring systems.

Nonetheless, this study also has some limitations. First, the evaluation of upper limb edema was based on clinical observation without standardized quantification (eg, grading severity, distribution, or pitting characteristics), which may introduce variability among operators. Additionally, since participants were recruited from a single-center ED using a convenience sampling strategy, there is a risk of sampling bias, which may affect the generalizability of the findings. Moreover, clinician variability in assessing edema, due to differences in experience or subjective interpretation, may have introduced assessment bias. Second, as this was a secondary analysis of an existing database, nurses' perceptions and experiences regarding the clinical utility of including edema in venous access assessments were not collected, limiting the ability to explore the practical implications of this finding from the nursing perspective. Third, while the findings support the inclusion of edema in the assessment of DIVA, the study was conducted in a single-center ED setting, which may limit generalizability to other clinical environments or populations. Finally, the study design did not allow for longitudinal follow-up to assess the impact of edema on catheter dwell time, complication rates, or patient outcomes beyond the cannulation procedure.

CONCLUSION

Upper limb edema is an independent predictor of DIVA, correlating with more cannulation attempts and greater use of ultrasound guidance. Its ease of bedside detection supports its inclusion in the EA-DIVA score and decision-making algorithms. A binary screening item, such as bilateral edema, may help triage patients directly to ultrasound-guided access. This approach warrants validation through future prospective studies.

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