· Review ·

Meta-analysis and systematic review of the incidence and influencing factors of acute skin failure in ICU patients

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Abstract

Objective To systematically evaluate the incidence of acute skin failure (ASF) and influencing factors among patients in the intensive care unit (ICU).

Methods Cohort studies investigating the incidence and determinants of ASF in ICU patients were systematically searched in PubMed, Cochrane Library, Web of Science, Embase, China National Knowledge Infrastructure, Wanfang Database, CQVIP, and China Biology Medicine from database inception to August 31, 2025. A meta-analysis was performed using R software.

Results Ten studies involving 2,870 participants were included in the meta-analysis. The pooled incidence of ASF among ICU patients was 38.4% (95% *CI:* 0.246–0.545). Subgroup analysis indicated significant regional differences in ASF incidence (P<0.001). Meta-regression analysis demonstrated that sample size (β=−0.001), study design (β=1.353), and publication year (β=−1.114) were significantly associated with the effect size. Furthermore, pooled analyses identified sepsis (*OR*=2.72), renal failure (*OR*=2.88), use of vasoactive agents (*OR*=3.31), and use of sedative and analgesic medications (*OR*=5.15) as significant factors associated with ASF occurrence.

Conclusion ASF is common among ICU patients. Sepsis, renal failure, and the use of vasoactive agents and sedative-analgesic medications may be associated with an increased risk of ASF, providing a basis for early identification and targeted interventions in clinical practice. However, given the substantial heterogeneity among the included studies, these findings require further validation.

Keywords: intensive care unit, acute skin failure, meta-analysis, systematic review, nursing

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Introduction

Acute skin failure (ASF) is defined as a cutaneous and subcutaneous tissue death event caused by inadequate perfusion due to hemodynamic instability and reduced tissue tolerance[1]. Patients in the intensive care unit (ICU) are particularly susceptible to ASF due to complex medical conditions, frequent complications, and common comorbidities, such as low tissue perfusion status, malnutrition, infection, and prolonged bed rest[2]. At present, there is no universally accepted diagnostic standard for ASF. Considerable variation among studies regarding diagnostic criteria and assessment procedures has led to substantial discrepancies in the reported incidence of ASF among ICU patients, ranging from 14.46% to 83.7%, with limited consistency and comparability[3,4]. ASF can result in a significantly prolonged hospital stay, increased mortality risk, and worsened prognosis[5]. In addition, because the clinical manifestations of ASF are highly similar to those of pressure injuries (PI), ASF is easily misdiagnosed as a nursing-related adverse event in clinical practice, thereby imposing considerable psychological burden and occupational stress on nursing staff [6,7]. Despite increasing studies of the incidence and risk factors for ASF in recent years, the inconsistencies in diagnostic standards, heterogeneity in study populations, and variations in study design and methodology have made it difficult to draw conclusions and establish strong clinical guidelines. Therefore, in this study, a systematic review was conducted to synthesize the current evidence and clarify the incidence and key determinants of ASF in ICU patients, with the aim of providing scientific evidence for the early identification of high-risk populations, development of targeted preventive strategies, and promotion of standardized ASF assessment and risk management in clinical practice.

Materials and Methods

Materials

Literature Search: A computerized literature search was conducted using the English-language databases PubMed, Cochrane Library, Web of Science, and Embase as well as the Chinese-language databases CNKI, Wanfang Database, CQVIP, and CBM. Studies reporting the incidence of and risk factors for ASF were collected. The search period covered the inception of each database up to August 31, 2025 and the search was limited to publications in Chinese or English. To avoid missing potentially relevant studies that did not explicitly mention “ICU” in their titles or abstracts, “ICU” was not used as a search restriction term. English search terms included “acute skin failure,” “skin failure,” and “terminal skin failure.” Chinese search terms included “急性皮肤衰竭” (acute skin failure) and “皮肤衰竭 (skin failure).” Manual searches were performed as a supplement. Because ASF-related MeSH terms or Emtree terms are currently unavailable, free-text terms were used for the search. Using PubMed as an example, the search strategy was as follows: (acute skin failure[Title/Abstract]) OR (skin failure[Title/Abstract]) OR (terminal skin failure[Title/Abstract]). The detailed search strategy is presented in Table S1.

This study followed the PRISMA 2020 reporting guideline for systematic reviews and has been preregistered with PROSPERO (registration number: CRD420251038549). Further registration details can be accessed at https://www.crd.york.ac.uk/prospero/.

Inclusion and Exclusion Criteria: The inclusion criteria were as follows. (1) The study population consisted of ICU patients aged ≥18 years. (2) The study reported the incidence of ASF. If influencing factors were investigated, multivariate analysis results (e.g.,

the odds ratio [OR] and 95% confidence interval [95% CI]) or raw data allowing for the calculation/conversion of effect sizes were required. (3) A cohort study design was used. (4) Clearly defined ASF diagnostic criteria (including clinical definitions, characteristics of skin lesions, and relevant hemodynamic indicators) were included to facilitate the assessment of inter-study heterogeneity. The exclusion criteria were as follows: (1) duplicate publications or studies with data originating from the same patient population, (2) data that could not be extracted, and (3) articles not published in Chinese or English. The literature screening flow diagram is shown in Figure 1.

Methods

Literature Screening: Two researchers independently used NoteExpress software to deduplicate and preliminarily screen the retrieved literature. They then independently extracted data from the included studies, followed by cross-verification. In the event of disagreements, a third researcher was consulted to participate in the discussion and make the final judgment.

Quality Assessment and Data Extraction: The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the included studies. The NOS contains eight items covering three domains: selection of study groups, comparability of the groups, and ascertainment of the outcome. The maximum total score is 9 points, and scores of 0–3 indicate low quality, 4–6 indicate moderate quality, and ⩾7 indicate high quality. Two researchers independently performed the quality assessment and cross-verification. Disagreements were resolved through discussion and consensus, with the involvement of a third researcher as needed. The extracted items included the first author, publication year, study population, country where the study was conducted, study design, sample size, ASF diagnostic method, ASF incidence, and reported influencing factors.

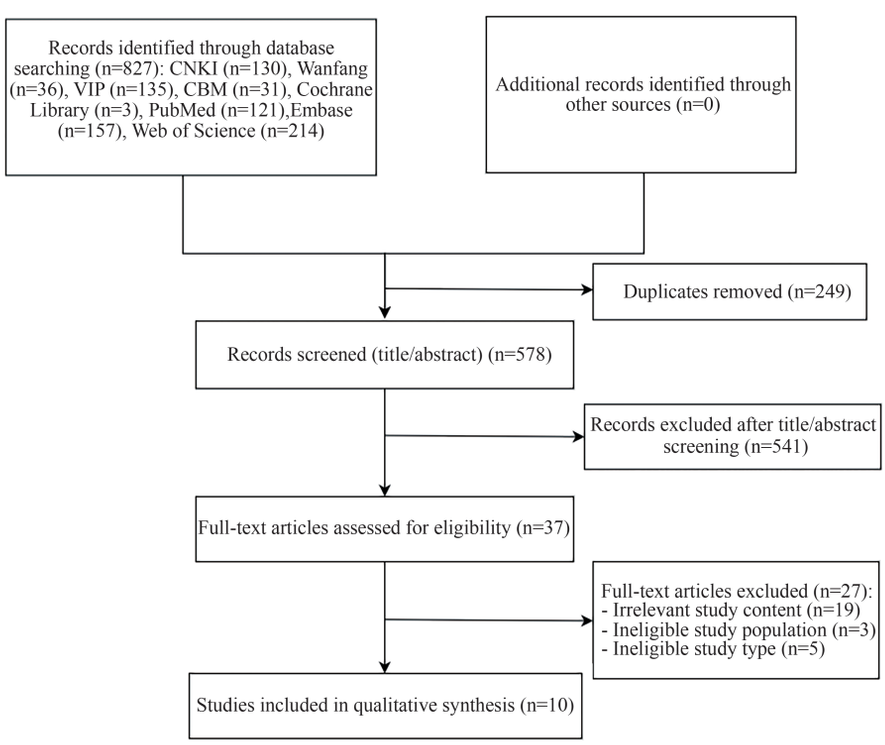


Figure 1. Flow diagram of the literature screening process.

Statistical Methods

Statistical analyses were performed using R software (version 4.2.2). For the pooled incidence of ASF, a generalized linear mixed model (GLMM) with a logit link function was applied using a one-step approach. To identify influencing factors, risk factors reported in at least two studies were included in the meta-analysis. *OR*s and corresponding 95% *CI*s reported in individual studies were extracted. Standard errors were calculated after logarithmic transformation, and pooled effect sizes were estimated using the inverse variance method under a random-effects model, with between-study variance (τ^2) estimated using the restricted maximum likelihood (REML) method.

Considering the potential differences in study populations, diagnostic criteria, and methodologies among studies, random-effects models were applied throughout the analyses. Heterogeneity across studies was assessed using Cochran's Q test (α=0.10) and the I^2 statistic. I^2 values of <25%, 25%–50%, 50%–75%, and >75% were considered to indicate low, moderate, high, and considerable heterogeneity, respectively. When substantial heterogeneity was observed (I^2>50%), subgroup analyses and meta-regression analyses were conducted to explore potential sources of heterogeneity. A sensitivity analysis was performed using a leave-one-out approach to assess the robustness of the results. When at least 10 studies were included, publication bias was initially assessed using funnel plots and further quantified using Egger's regression test. All statistical tests were two-sided, and a value of P<0.05 was considered statistically significant.

Results

General Characteristics

In total, 827 records were identified through the database search. After removing duplicates, 578 records remained. Following the initial screening of titles and abstracts, 37 articles were selected for full-text assessment. Ultimately, 10 studies [3,4,8–15] met the inclusion criteria, including 7 identified as high quality [3,4,8–11,14] and 3 identified as moderate quality [12,13,15]. The studies involved 2,870 patients, of whom 847 developed ASF. All 10 studies [3,4,8–15] reported the incidence of ASF in ICU patients, and 5 studies [3,9,10,12,13] provided multivariate-adjusted *ORs* with 95% *CIs* for factors influencing ASF in ICU patients. The basic characteristics of the included studies are detailed in Table 1, and methodological quality assessment results are shown in Table S2.

Meta-analysis Results

Overall incidence of acute skin failure in ICU patients: A meta-analysis of the 10 studies meeting the inclusion criteria showed that the pooled incidence of ASF among ICU patients was 38.4% (95% *CI:* 0.246–0.545). Considerable heterogeneity was observed across studies (I^2=96.5%, P<0.001). The results are presented in Figure 2.

Influencing factors for ASF in ICU patients

Concurrent sepsis and renal failure

Three studies [9,12,13] reported the effect of concurrent sepsis on ASF. The pooled analysis showed that concurrent sepsis was significantly associated with the occurrence of ASF [*OR*=2.72, (95% *CI* 1.69–4.36), P< 0.001], with no significant heterogeneity among studies (I^2=0%, P=0.736). Two studies [9,13] reported the effect of concurrent renal failure on ASF. The pooled analysis indicated that concurrent renal failure was significantly associated with ASF occurrence [*OR*=2.88, (95% *CI* 1.59–5.22), P<0.001], and no significant heterogeneity was detected across studies (I^2=0%, P=0.996).

Table 1. Basic characteristics and quality assessment of included studies.

Author (Year)	Country	Study design	Sample size	Study population	ASF diagnostic criteria	ASF incidence (%)	Influencing factors
Liu [11] (2025)	China	A	150	ICU patients with septic shock	①, ②, ③	23.30%	-
Xu [9] (2025)	China	A	80	ICU patients aged ⩾ 80 years	④	41.00%	BMI, renal failure, sepsis, sedative/analgesic drugs, NRS2002 score, Braden score
Tang [10] (2025)	China	A	254	ICU patients with sepsis	At least one of ④, ⑤ > 2s, ⑥, ⑦ plus concurrent ① and ②	35.00%	Peripheral artery disease, mechanical ventilation, vasoactive agents, APACHE-II score, mean arterial pressure, lactate level
Zhang [8] (2025)	China	B	217	General ICU patients	Any one of ④, ⑤ > 3s, ⑧ plus concurrent ②	23.04%	-
Zhu [12] (2024)	China	B	204	General ICU patients	①, ②	28.43%	Age, sepsis, vasoactive agents, peripheral perfusion index, serum albumin level
Zhang [14] (2024)	China	B	1036	General ICU patients	Any one of ③, ④, ⑤ > 3s, ⑧	24.32%	-
Xu [13] (2024)	China	B	251	ICU patients aged ⩾ 65 years	At least one of ④, ⑤ > 2s, ⑧ plus concurrent ① and ②	41.83%	Braden score, renal failure, heart failure, sepsis, lactate level, sedative/analgesic drugs
Wang [3] (2024)	China	A	491	ICU patients with septic shock	Any one of ④, ⑤ > 2s, ⑥, ⑦, ⑧	14.46%	Body surface area, NEWS score, SOFA score, lactate level, peripheral perfusion index, capillary refill time
Wang [4] (2022)	China	A	123	ICU patients with septic shock	Any one of ④, ⑤ > 2s, ⑥, ⑦, ⑧	83.70%	-
Greenway [15] (2021)	USA	A	64	ICU patients with COVID-19-positive status	-	79.70%	-

Notes: A: Retrospective cohort study; B: Prospective cohort study. ① Ischemia due to poor blood perfusion (e.g., cyanosis, gangrene of fingers or toes, or skin blister formation, typically purple, yellow, or black in color); ② Relatively rapid disease progression. Most lesions are not associated with bony prominences and often appear pear-shaped, butterfly-shaped, or horseshoe-shaped; ③ Skin perfusion pressure ⩽ 25 mmHg; ④ Skin mottling score > 0; ⑤ Capillary refill time; ⑥ After excluding non-circulatory factors, severe anemia, and other blood disorders, the patient's fingertip transcutaneous oxygen saturation decreases by >5%; ⑦ Decreased skin sensation; ⑧ Cold and clammy skin: ambient temperature 18–22 ℃, humidity 55%–65%, body surface temperature measured using an infrared thermometer of <33.5 ℃ in the absence of physical cooling, accompanied by moist skin. ASF: acute skin failure; NRS2002 score: Nutritional Risk Screening 2002 score; Braden score: Braden Scale for Predicting Pressure Sore Risk score; NEWS: National Early Warning Score; SOFA: Sequential Organ Failure Assessment score; APACHE II score: Acute Physiology and Chronic Health Evaluation II score.

Use of vasoactive agents and sedative/analgesic drugs

Two studies [10,12] reported the effect of vasoactive agent use on ASF. The pooled results demonstrated that the use of vasoactive agents was significantly associated with the occurrence of ASF [*OR*=3.31, 95% *CI* (1.64–6.68), *P*=0.001], with moderate heterogeneity observed across studies (I^2=36.9%, *P*=0.208). Two studies [9,13] reported the effect of sedative/analgesic drug use on ASF. The pooled analysis showed that the use of sedative/analgesic drugs was significantly associated with ASF occurrence [*OR*=5.15, 95% *CI* (1.35 – 19.64), *P*=0.016], with substantial heterogeneity detected among studies (I^2=58.7%, *P*=0.120).

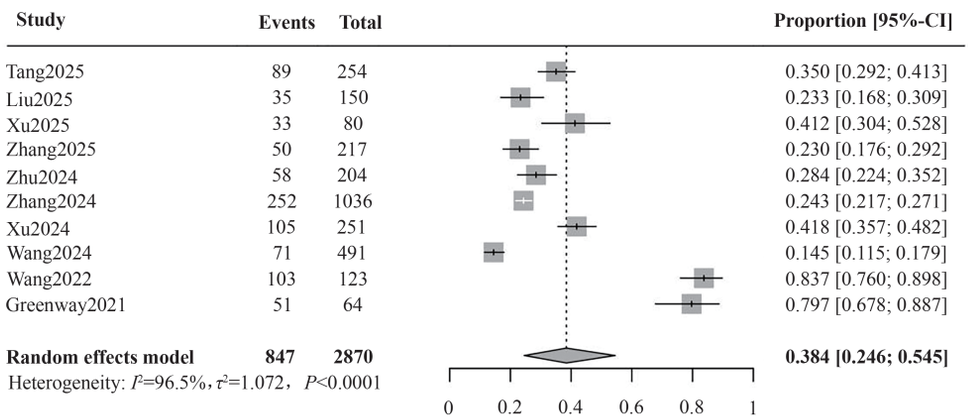


Figure 2. Forest plot of the incidence of ASF in ICU patients.

Lactate level and peripheral perfusion index

Three studies [3,10,13] reported the effect of lactate level on ASF. In a meta-analysis, lactate levels were not significantly associated with the risk of ASF occurrence [*OR*=2.16, 95% *CI* (0.70–6.70), *P*=0.183], and there was considerable heterogeneity among studies (I^2= 93.3%, *P*<0.001). Two studies [3,12] reported the effect of the peripheral perfusion index on ASF. The pooled results indicated that the peripheral perfusion index was not significantly associated with the risk of ASF occurrence [*OR*=0.04, (95% *CI*: <0.01–4.80), *P*= 0.189], with considerable heterogeneity observed across studies (I^2=91.8%, *P*<0.001).

Subgroup analysis and meta-regression analysis

Subgroup analyses of ASF incidence were conducted according to study design, sepsis status, age group, and geographic region. The pooled incidences of ASF in retrospective cohort studies and prospective cohort studies were 41.2% (95% *CI*: 0.195–0.670) and 34.9% (95% *CI*: 0.280–0.427), respectively, with no significant between-group heterogeneity (*Q*=0.22, *P*=0.642). The pooled incidences of ASF among patients with and without sepsis were 38.7% (95% *CI*: 0.243–0.554) and 37.8% (95% *CI*: 0.146–0.684), respectively, with no significant between-group heterogeneity (*Q*=0.00, *P*=0.959). The pooled incidences of ASF among patients aged ⩾60 years and <60 years were 41.7% (95% *CI*: 0.365–0.471) and 37.8% (95% *CI*: 0.212–0.579), respectively, with no significant between-group heterogeneity (*Q*=0.14, *P*=0.706). The pooled incidences of ASF in studies conducted in China and the United States were 33.9% (95% *CI*: 0.221–0.481) and 79.7% (95% *CI*: 0.681–0.878), respectively, with significant between-group heterogeneity observed (*Q*=22.7, *P*<0.001).

Meta-regression analysis was performed by including publication year, sample size, study design, sepsis status, age group, and geographic region as covariates. Sample size (β=−0.001, *P*=0.024), study design (β= 1.353, *P*=0.013), and publication year (β=−1.114, *P*< 0.001) were significantly associated with the effect size. Residual heterogeneity remained substantial after meta-regression (I^2=79.2%).

Sensitivity analysis and publication bias

The results of a sensitivity analysis showed that after sequentially excluding each study, the pooled incidence of ASF ranged from 0.329 to 0.420, with highly overlapping confidence intervals, indicating that the overall results were stable and reliable. Visual inspection of the funnel plot showed that most studies were distributed on both sides of the central axis, although some

asymmetry in the distribution of study estimates was observed (Figure 3). Egger's regression test yielded a *P*-value of 0.066, suggesting a lack of significant publication bias.

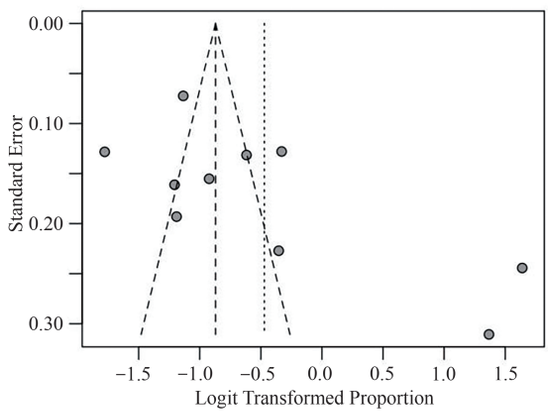


Figure 3. Funnel plot of the incidence of ASF in ICU patients.

Discussion

The present study demonstrated that ASF may represent a relatively common skin complication in critically ill patients, with a pooled incidence of 38.4% among ICU patients. However, considerable heterogeneity was observed across studies (I^2=96.5%); therefore, these findings should be interpreted cautiously within the context of study characteristics and clinical settings.

Meta-regression analysis indicated that sample size, study design, and publication year were significantly associated with effect size. The negative association between sample size and effect size suggests that smaller studies are more likely to report higher incidence estimates. With respect to study design, it is possible that prospective studies allow continuous and dynamic patient monitoring, potentially improving ASF detection rates, whereas retrospective studies rely primarily on medical records and may therefore be more susceptible to information bias. In addition, the negative association between publication year and effect size may be related to the increasing awareness of ASF and ongoing improvements in critical care management strategies. Notably, a subgroup analysis demonstrated significant regional differences in ASF incidence; however, these findings should be interpreted with caution. International data included in this study were derived from a single study involving patients with COVID-19 conducted during the pandemic period [15]. Critically ill patients with COVID-19 frequently present with systemic inflammatory responses, microcirculatory dysfunction, and coagulation abnormalities, all of which may increase the risk of impaired skin perfusion [16]. Therefore, regional differences observed in this study may have been influenced by specific disease characteristics.

Substantial residual heterogeneity remained after meta-regression (I^2=79.2%), indicating that additional unexplained sources of heterogeneity may exist. This may be attributable in part to the lack of a standardized diagnostic framework for ASF. As an emerging concept introduced in recent years, universally accepted diagnostic criteria for ASF are lacking, resulting in inconsistencies in case identification across studies [17]. Most studies have relied on a combination of skin manifestations, tissue perfusion indicators, and relevant clinical features for diagnosis. Variation in the criteria used to identify ASF may influence incidence estimates and reduce comparability across studies. Therefore, establishing standardized diagnostic criteria and risk assessment tools for ASF may be necessary to improve consistency across studies and facilitate early clinical identification and targeted interventions.

In a pooled analysis, concurrent sepsis and renal failure were significantly associated with ASF occurrence. These findings are generally consistent with those reported by Savage et al. [18], who observed that 80.8% of patients with ASF had sepsis and 76.9% experienced acute kidney injury. Similarly, Curry et al. [19] reported

that all patients with ASF had at least two organ dysfunctions or a single organ failure combined with sepsis at the time of diagnosis. One possible explanation is that infection-induced systemic inflammatory responses substantially impair microcirculatory function, leading to inadequate tissue perfusion, imbalance between oxygen supply and demand, and ultimately tissue injury and organ dysfunction [20]. In addition, under severe physiological stress, compensatory mechanisms generally prioritize blood flow to vital organs, such as the brain, heart, and kidneys, while perfusion to peripheral tissues including the skin may be further reduced, thereby increasing susceptibility to ASF.

The use of vasoactive agents and sedative/analgesic drugs was significantly associated with ASF occurrence. Mileski et al. [21] identified several medications associated with ASF development, including norepinephrine, fentanyl, morphine, and propofol. There is evidence that vasoactive agents may reduce tissue perfusion and restrict capillary blood flow through vasoconstriction. Moreover, certain sedative and analgesic agents may impair vasomotor regulation and attenuate compensatory microcirculatory responses to ischemic conditions. These mechanisms may collectively contribute to the development and progression of ASF [22].

Distinguishing ASF from PI remains a major challenge in clinical practice. Previous studies have described ASF as an “unavoidable PI” or “critical illness-related PI” [23,24]. However, increasing evidence suggests that ASF and PI differ fundamentally in both pathological mechanisms and clinical characteristics. PI is primarily caused by external factors, including prolonged pressure, shear forces, and friction, and commonly occurs over bony prominences, such as the sacrum and heels. In contrast, ASF typically occurs in the context of critical illness and results from hemodynamic instability and tissue hypoperfusion, representing a cutaneous manifestation of systemic pathological processes [7]. Because of overlapping clinical presentations, ASF may be misdiagnosed as PI and consequently regarded as a preventable nursing adverse event, thereby increasing management burden and potentially affecting accurate skin injury management. Therefore, focusing on ASF incidence and associated factors among ICU patients may contribute to improving differential diagnosis between ASF and PI and facilitating early identification and targeted interventions for high-risk critically ill populations.

This study had several limitations. First, there was substantial differences among included studies in terms of diagnostic criteria, study populations, and regional characteristics. Although meta-regression was conducted to explore potential sources of heterogeneity, subgroup analyses based on diagnostic criteria could not be performed owing to the limited number of studies; therefore, heterogeneity may not have been fully explained. Second, most included studies were single-center studies with relatively small sample sizes. The lack of large multicenter prospective studies may limit the representativeness and generalizability of the pooled incidence estimate. Third, the number of included studies was limited, and evidence regarding several associated factors remained insufficient; therefore, the stability of these findings requires further confirmation.

Conclusion

ASF appears to be relatively common among ICU patients. Sepsis, renal failure, and the use of vasoactive agents and sedative-analgesic medications may be associated with ASF occurrence. Future studies should focus on establishing standardized diagnostic criteria and developing early warning tools to improve the identification of high-risk populations.

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Author contributions

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Conflict of interest

All authors declare no conflicts of interest.

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