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Treating shock with norepinephrine administered in midline catheters in an intermediary care unit: a retrospective cohort study

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ABSTRACT

Objectives A rising incidence of septic shock as well as recommendations for early vasopressor initiation has increased the number of patients eligible for norepinephrine (NE). Traditionally, NE has been administered through central lines, in intensive care units, due to the risk of extravasation in peripheral lines. The aim of the current study is to determine the rate of complications and patient outcomes when NE is administered through midline catheters (MCs) in intermediary care units (IMCUs).

Design Retrospective cohort study.

Setting Three IMCUs in southern Sweden

Participants Patients with septic shock who received NE through a MC from September 2020 through March 2023.

Primary and secondary outcome measures The primary outcome was a major complication to treatment, defined as extravasation of NE, catheter-associated venous thromboembolism and catheter-associated bloodstream infection (BSI). Secondary outcomes included patient outcomes after intermediary care (either deceased, discharged to regular ward care or intensive care) and the need for additional central lines.

Results Of 474 eligible patients, 472 were included, with a median (IQR) age of 73.5 (65–80) years, with 281 (60%) men. The median (IQR) duration of NE infusion was 21 (9–38) hours, with a median (IQR) dosage of 0.12 (0.08–0.20) µg/kg/min. Major complications occurred in 12 cases (2.5%), with one suspected extravasation, seven thromboembolic events and four catheter-related BSIs. After intermediary care, 334 patients (71%) were discharged to regular ward care, 66 patients (14%) were escalated to intensive care and 72 (15%) died in intermediary care, of whom 69 had a documented ceiling of care decision. 100 patients (21%) received a central line.

Conclusion NE administration in MCs was associated with a low rate of short-term complications and could decrease the need for central lines. MCs can enable the initial management of circulatory failure outside intensive care, but more studies are needed to determine the long-term value of IMCUs.

Trial registration number NCT06121115.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study includes a large real-life cohort, larger than previous studies evaluating norepinephrine in midline catheters.
⇒ A prespecified and published protocol with well-defined and clinically relevant endpoints was used.
⇒ However, the study is retrospective and reliant on clinical documentation in medical records.
⇒ External validity may be limited regarding patient outcomes as these are dependent on the local healthcare organisations.

INTRODUCTION

Norepinephrine (NE) is a cornerstone drug in the management of circulatory failure and the preferred vasopressor for septic shock.[1 2] Epidemiologic studies suggest an increasing caseload of patients with severe infections due to population ageing, increasing immunosuppression and surgical procedures.[3 4] Concurrently, an early vasopressor initiation with a more restrictive fluid resuscitation has been suggested.[5–7] Thus, the number of patients eligible for NE treatment is likely to increase, which may come to burden intensive care units (ICUs).

Traditionally, central venous catheters (CVCs) have been preferred over peripheral venous catheters (PVCs) for NE administration due to concern of tissue ischaemia in case of extravasation.[8 9] However, central venous catheterisation is typically only performed by certain physicians, which may delay placement in many hospitals, especially after office hours. In addition, central venous catheterisation is associated with mechanical complications as well as bloodstream infections (BSI).[10] Recently, the use of midline catheters (MCs), longer indwelling peripheral catheters inserted in the upper arm, has increased substantially.[11 12] Midline insertion

is easier to learn and is often performed by nursing staff. Mechanical complications are less frequent than in CVCs, although long-term complications include thrombosis and BSIs.[13 14]

Only a few studies have evaluated complications of vasopressor administration in MCs, all in the ICU setting.[15–17] At our centre, patients with septic shock are often initially treated outside the ICU, in intermediary care units (IMCUs), with NE administered through MCs. The aim of the current study is to evaluate this routine to determine complication rates, as well as patient outcomes.

MATERIAL AND METHODS

This is a retrospective study using chart reviews to ascertain data on clinical characteristics and outcomes. The outcomes were prespecified, and the study protocol was registered in advance at clinicaltrials.gov (NCT06121115). The population of interest was the patients receiving NE in MCs in IMCUs at Skåne University Hospital in southern Sweden, with centres in the cities of Malmö and Lund. The protocol was reviewed and agreed upon by the authors, who are all medical doctors working at the included IMCUs, before the study. Chart review was performed by HK, AA and GT.

The intermediary care at Skåne University Hospital is provided by three units, organised by the Internal Medicine and the Infectious Diseases departments. The IMCUs are characterised by a higher staff density than a regular hospital ward, with a nurse-to-bed ratio of 1:2. The majority of patients are admitted from the nearby emergency departments, often directly from the resuscitation room. The criteria for admission to the IMCU is any patient deemed to be too unstable to be cared for in a regular hospital ward but not requiring immediate ICU care. All admissions are approved by the responsible IMCU physician. Treatment options include non-invasive ventilation, arterial catheters for continuous blood pressure measurements, point-of-care ultrasound and vasopressor drugs, but invasive ventilation and continuous renal replacement therapy are not available. The length of stay in the IMCUs is typically short with patients either stabilising and being moved to regular wards or deteriorating, leading to ICU escalation. Daily conferences involving the responsible IMCU physician and a specialist in intensive care are held where all patients' treatment strategies are evaluated. A decision whether the patient should have a ceiling of care or not (most commonly no ICU escalation/no cardiopulmonary resuscitation) should be documented upon IMCU admission. The ceiling of care decisions are made by the responsible physician who confers with both another colleague and the patient/next of kin.

MC procedures

Unless there is a specific reason not to, patients in the IMCUs receive a MC upon arrival, a single-lumen, 10 cm polyurethane catheter (BD PowerGlide Pro), with a diameter of 18 or 20 G (external diameter of ~1.3 or 1.1 mm). The MC is placed under sterile conditions in either the brachial, cephalic or basilic vein by a specially trained nurse or doctor, using ultrasound guidance, 24 hours a day. After insertion, the MC is fixated with a StatLock Pro fastening device and an adhesive film. To maintain functionality for up to 29 days, the MC is flushed with 20 mL of 0.9% saline at a minimum of three times a day. The nurse inspects the insertion site and positioning of the catheter and tests its functionality by flushing it at the beginning of each shift. The site of insertion, size, time for insertion and removal, as well as any complications and functionality are all documented.

NE administration

Patients with circulatory failure typically receive fluid resuscitation before IMCU admission and are then started on vasopressors in MCs in the IMCU. However, a minority of patients may start peripheral vasopressors in the resuscitation room, with a change of the route for NE administration to the MC after its placement. The initiation of NE infusion is accompanied by the placement of an arterial line for continuous blood pressure measurements and a urinary catheter to monitor urinary output. No other pharmacological substances are concomitantly administered through the MC. NE is diluted in saline to a final concentration of 40 µg/mL and intravenously administered through a syringe pump. If the dose reaches 0.2 µg/kg/min, the attending ICU consultant is contacted to discuss further level of care, often resulting in ICU transfer. During the administration of NE, the catheter insertion site is observed regularly to detect signs of extravasation and findings are routinely documented in medical records. In case of extravasation, 10–15 mL phentolamine at a concentration of 0.6 mg/mL is carefully infiltrated in the affected area to reverse the effect of NE, and the patient is closely monitored.

Participants

All hospitalisation episodes where the patient had received an MC and treatment with NE in an IMCU at Skåne University Hospital between 01 September 2020 and 31 March 2023 were eligible for chart review. The unit of interest was an episode with circulatory failure and an individual could be included in several episodes if discharged from the hospital between the episodes. If a patient had a concurrent central line and no documentation of NE being administered through the MC, we assumed that NE would have been administered through the central line and the patient was not included. Patients who had actively made their medical files inaccessible were excluded.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting of the research.

Definitions

All variables and definitions are found in the online supplemental study protocol . The baseline was defined as the time that NE was initiated. Vital signs were recorded according to local clinical routine using the National Early Warning System 2 (NEWS2) Score, registered respiratory rate, blood pressure, mental alteration, heart rate, fever, oxygen saturation and whether supplemental oxygen was given.[18] Collected laboratory values included creatinine, C reactive protein and lactate. Acute kidney injury was defined as a creatinine>100 mmol/L without documented pre-existing kidney disease. In addition, we recorded blood cultures taken at baseline and their results. For the MCs, the side of insertion, size and catheter dwell time were recorded. For NE, the maximum dose (µg/kg/min) was documented, along with treatment duration (hours). If the patient received NE administered through a CVC after MC, this was not included in the duration. The ceiling of care decisions documented from hospital admission to the end of IMCU care were recorded. Whether the circulatory failure had been caused by an infection was evaluated by the authors after reviewing all available data.

Outcomes

A major complication (the primary outcome) was defined as a complication with a high risk of permanent complications and/or prolonged hospitalisation, based on clinical judgement. The primary outcome was a composite, defining a major complication as any of:

- Suspected or confirmed *extravasation* of NE administered in MC: any of the following: (1) symptoms including pain, pallor, induration, swelling, coldness, mottling, blistering or necrosis described in the midline area, (2) the use of an antidote (phentolamine) or (3) the need for surgical revision.
- *Midline-associated bloodstream infection* (*MLABSI*): a primary BSI with the growth of a relevant organism in blood cultures in a patient who had had a midline within the 48-hour period before the development of the BSI. The BSI should not be explained by infection elsewhere.
- *Midline-associated deep vein thromboembolism*: Any deep vein thrombosis in the midline area or pulmonary embolism. Thromboembolism had to be verified by ultrasound or radiology, up until 30 days after MC insertion. In the case of pulmonary embolism, this was considered midline associated in any case where there was no other documented focus for this, such as concurrent lower limb deep vein thrombosis (DVT).

All instances of a potential primary outcome (major complication) were reviewed independently by two reviewers (HK or AA with GT).

The secondary outcomes included:

- Patient outcomes: length of stay in IMCU, discharge destination from IMCU (to the regular hospital ward, escalation to ICU or deceased in IMCU), ICU length of stay, hospital length of stay and in-hospital mortality.
- Minor complications related to MC use: dislodgement of the MC, suspected infiltration of non-vesicant medications, loss of function/occlusion, local irritation or other.
- Outcomes of the MC: premature removal due to a complication, the need for a central line or the need for multiple midlines.

Analysis

The data are presented using medians with IQRs for continuous variables and frequencies for categorical ones. In the case of missing values, complete case analysis was performed, except for complications where missing was considered as 'no complication'. However, in the estimation of the total NEWS2 Score, any missing values were considered normal. No statistical hypothesis testing was performed. To facilitate comparisons with other settings, complication rates were described using absolute frequencies as well as rate per 1000 catheter days.

RESULTS

In total, we identified 474 cases that had received NE in a MC in an IMCU at Skåne University Hospital from 1 September 2020 to 31 March 2023. Two cases were excluded due to charts being unavailable, leaving 472 episodes in 461 unique individuals (9 patients had two episodes and 1 patient had three episodes) for review. The median age was 73.5 (IQR: 65–80) years, and 281 patients (60%) were men. Of all patients, 172 (37%) had functional impairment before the hospitalisation (home care or living in an institution). Comorbidities were present in 398 patients (85%), with 284 having two or more comorbidities and 135 patients three or more. In total, 229 (49%) had a documented ceiling of care (see table 1).

At baseline, the patient's vital signs were affected, with a median (IQR) mean arterial pressure of 60 (55–67) mm Hg, and a median (IQR) NEWS2 Score of 8 (6–10) points, although NEWS2 registrations were often incomplete (see table 2). Laboratory values showed a lactate increase>2.0 mmol/L in 259 patients (55%), an increase in C-reactive protein (CRP) of >5 mg/L in 443 (94%) and acute kidney failure in 293 (62%). Blood cultures were taken within 48 hours of baseline in 418 patients (89%), with a positivity rate of 190/418 (45%). The most commonly isolated species were *Escherichia coli* and *Staphylococcus aureus*, with 29% and 14%, respectively.

Of 470 patients with insertion side documented, 257 (55%) had received an MC in the right arm and 213 (45%) in the left arm. In 443 patients with specific veins documented, the basilic vein was preferred, with 305 (69%) of MCs, with 95 (21%) and 43 (10%) being placed in brachial and cephalic veins, respectively. All patients received 10 cm long MCs, with 98% and 2% receiving 18 G and 20 G diameters, respectively. The total observation time was 3137 catheter days, with an individual median of 6 days (range: 0–29 days). In total, NE was administered

Table 1 Baseline characteristics

Demographics	
N	472
Age, median (IQR)	73.5 (65–80)
Female sex	191 (40%)
BMI (kg/m^2), median (IQR)	26 (23–31)
Comorbidities	
Chronic cardiac disease	246 (52%)
Chronic pulmonary disease	122 (26%)
Chronic renal disease	70 (15%)
Dialysis	18 (4%)
Active malignancy	92 (19%)
Diabetes mellitus	162 (34%)
Chronic hepatic disease	25 (5%)
Autoimmune disease	49 (10%)
Transplantation	8 (2%)
Previous VTE	67 (14%)
Predisposing factors	
Anticoagulants (DOAC/warfarin/LMH)	186 (39%)
Immunosuppression	67 (14%)
Central line before baseline*	17 (4%)
Functional status	
Home care	116 (25%)
Nursing home	56 (12%)
Ceiling of care	
No CPR	63 (13%)
No CPR or ICU escalation	166 (35%)

All results are presented as median (IQR) or n (%).
*These were central lines not used for norepinephrine infusion.
BMI, body mass index; CPR, cardiopulmonary resuscitation; DOAC, direct oral anticoagulants; ICU, intensive care unit; LMH, low-molecular weight heparin; VTE, venous thromboembolism.

Table 2 Acute episode characteristics

IMCU admission	
From emergency room	342 (72%)
In-hospital transfer	123 (26%)
Infectious cause of admission*	337/452 (75%)
Non-infectious cause of admission	115/452 (25%)
Vital signs at baseline	
Respiratory rate, n=416	22 (19–27)
Systolic, median (IQR), n=465	82 (73–90)
Diastolic, median (IQR), n = 420	50 (45–55)
MAP, median (IQR), n = 430	60 (55–67)
Mental alteration, n = 440	51 (12%)
Pulse, median (IQR), n = 434	95 (80–113)
Oxygen saturation, median (IQR), n = 452	94 (91–96)
Temperature>38.0°C, n = 396	87 (22%)
Supplemental oxygen, n = 455	302 (66%)
NEWS Score, median (IQR)†	8 (6–10)
Laboratory values	
Lactate, median (IQR)	2.2 (1.4–3.9)
Creatinine, median (IQR)	149 (104–233)
C reactive protein, median (IQR), n = 471	114 (37–231)
Length of stay (days)	
IMCU, median (IQR)	2 (1–4)
IMCU+ICU, median (IQR)	3 (2–5)
Hospitalisation, median (IQR)	9 (5–15)

All data are presented as median (IQR) or n (%). N=472 unless otherwise specified.
*Non-infectious causes include other reasons for shock, including pancreatitis, cholecystitis and cardiogenic shock, as assessed after chart review.
†NEWS was completed in 322 patients. Otherwise, in the calculation of the total NEWS Score, missing values have been considered normal.
ICU, intensive care unit; IMCU, intermediary care unit; MAP, mean arterial pressure; NEWS, National Early Warning System.

in MCs for 13 069 hours. The median duration of NE infusion was 21 hours, with a range of 0–206 hours. The median (IQR) peak dosage was 0.12 (0.08–0.20) µg/kg/min.

Complications

A major complication was registered in 12 patients (2.5%) (see table 3). Suspected extravasation occurred in 1 patient (0.2%) resulting in 0.08 events per 1000 hours of NE administration. In this episode, a suspected extravasation was specifically expressed in the medical record, due to leakage around the catheter site during NE infusion. The infusion was stopped, the patient was monitored closely and there was a change of line for NE infusion, but the patient did not develop symptoms and no further actions were needed. Although not the focus of the study, we identified five cases of extravasation in PVCs during the chart review (ie, when NE was administered in a PVC before MC placement). Thromboembolic events occurred in seven episodes (1.5%), corresponding to a rate of 2.2 thromboses per 1000 midline-days. These events were classified as four cases of DVT in the MC area and three cases of pulmonary embolism with no other explanation. In general, the patients with thromboses did not differ from the study population but catheter dwell times were longer and thromboses were confirmed on average 10 days after midline placement. In total, four MLABSI episodes were registered (0.8%), corresponding to a rate of 1.3 per 1000 catheter days. Cultures showed *S. aureus* in two cases, *Klebsiella variicola* and *Staphylococcus epidermidis*. Patients with MLABSI also had longer catheter dwell times and MLABSI events occurred after an average of 9 days. Of the 4 patients with suspected MLABSI, 3 patients had received multiple midlines and 2 patients had a concurrent CVC at the time of MLABSI.

Table 3 Complications and MC outcomes

Major complications	
Any major complication	12 (2.5%)
Extravasation	1 (0.2%)
Thrombosis	7 (1.5%)
MLABSI	4 (0.8%)
Minor complication	
Any minor complication	110 (23%)
Dislodgement	57 (12%)
Infiltration/leakage	9 (1.9%)
Occlusion	15 (3.2%)
Pain/irritation	29 (6.1%)
Other	6 (1.3%)
Midline outcomes	
Premature removal	110 (23%)
Multiple midlines	70 (15%)
CVC after midline	100 (21%)

All data are presented as n (%), with N=472. Premature removal refers to the unintended removal of the MC due to a complication, while venous access is still needed.
CVC, central venous catheter; MLABSI, midline-associated bloodstream infection.

A total of 110 MCs (23%) were associated with at least one minor complication, primarily accidental removals due to dislodgement. Nine patients experienced the infiltration of other substances than NE, which occurred after NE administration had been stopped. In total, 70 patients (15%) received multiple midlines, and 100 (21%) received a CVC after midline insertion at any time during the hospitalisation (see table 3).

Patient-related outcomes

Of the 472 patients, 334 (71%) patients were discharged to a ward, 66 patients (14%) were escalated to an ICU and 72 patients (15%) died in the IMCU (see figure 1). Of the patients who died in the IMCU, 69/72 (96%) had a documented ceiling of care. In total, 289 patients (61%) were transferred to a ward and later discharged alive, without ICU escalation. The median (IQR) IMCU length of stay (LOS) was 2 (1–4) days. For those admitted to ICU, the median (IQR) LOS was 4 (2–7.5) days. For the whole cohort, the median (IQR) of combined IMCU+ICU stay was 3 (2–5) days and the hospital LOS was 9 (5–15) days. The overall in-hospital mortality was 149, representing a case fatality risk of 32% (see figure 2).

DISCUSSION

This study evaluated complications and outcomes in patients with circulatory failure treated with NE administered through MCs in the IMCU. Major complications such as extravasation, thromboses and BSIs were rare in this population. Minor complications were more common, especially dislodgement of the catheter, often leading to premature removal. Only a minority of patients were escalated, with 14% being transferred to the ICU and 21% receiving a subsequent central line.

Among the major complications, we found one case of suspected NE extravasation. This is in line with previous

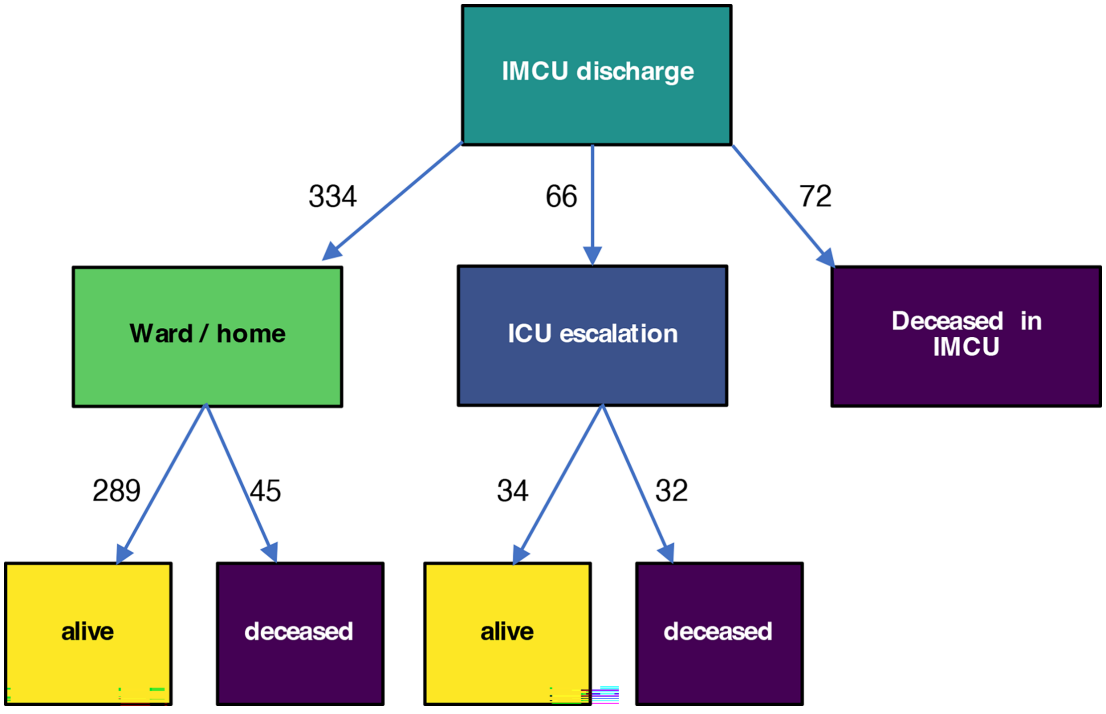

Figure 1 Patient outcomes after intermediary care and at hospital discharge. N=472. ICU, intensive care unit; IMCU, intermediary care unit.

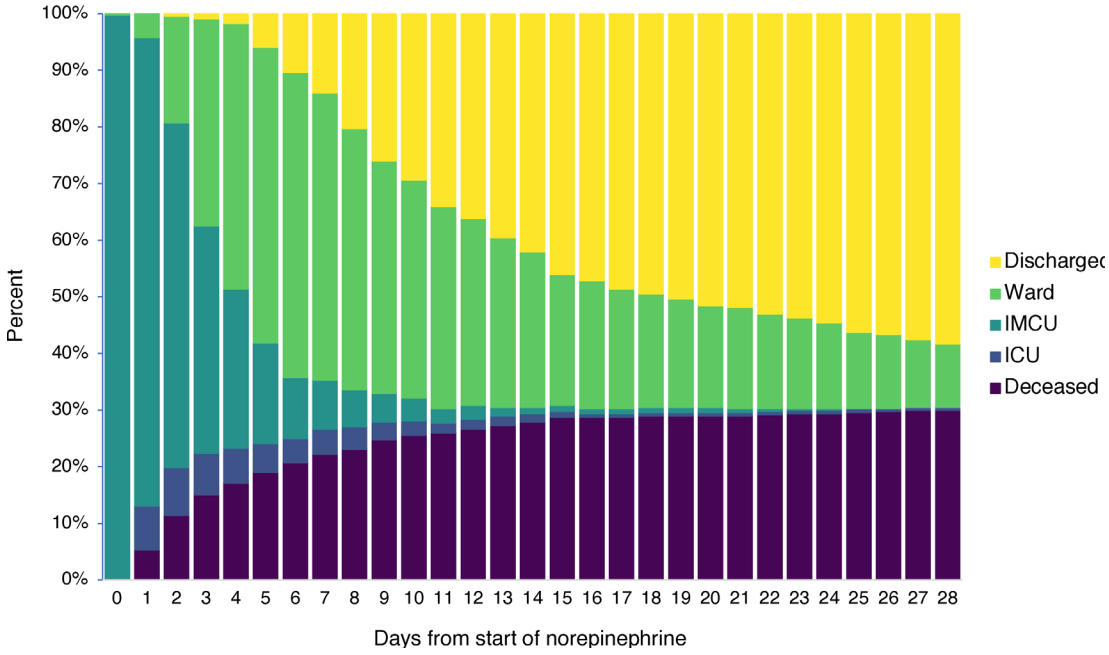

Figure 2 Patient outcomes the first 28 days after norepinephrine initiation, by patient location and day. All patients started at the IMCU at day 0. N=472. ICU, intensive care unit; IMCU, intermediary care unit.

studies, showing no extravasation in 203 patients and one extravasation in 248 patients.[15 17] These two earlier studies were conducted in ICUs, and one of them used a 20 cm MC, which makes it difficult to compare studies in detail. Infiltration of other substances occurred in nine cases, all of which were later in the hospitalisation episode. This suggests that the risk of accidental administration of medications into the tissue surrounding the catheter may increase over time. We also inadvertently noted five cases of extravasation of NE in PVCs. Unfortunately, we did not record the total number of patients receiving NE in PVCs before MC placement but from our experience, this would apply to a minority of patients. Since we lacked the denominator, we could not estimate the frequency of NE extravasation in PVC, but the five cases indicate a higher risk when NE is administered in PVCs than in MCs, also supported by previous studies showing an extravasation rate of 2–7%.[19–21]

Thrombotic events were confirmed in 1.5% of episodes, equivalent to 2.2 per 1000 catheter days, compared with 1.4–5% in previous studies.[11 22 23] A large meta-analysis of over 18 000 midlines showed a rate of 4% of thrombotic events.[12] The lower frequency in our study may be due to a shorter catheter dwell time of 6 days compared with 16.3 days. In addition, 39% had anticoagulants at baseline. Catheter-related BSIs were found in 0.8% of episodes or 1.3 per 1000 catheter days, in line with previous results, showing rates of <1% or 0–1 per 1000 midline days.[11 13 14 23] In CVCs, the frequency of BSI in CVCs has been estimated to be 1–2% in the ICU setting, with suggested higher rates outside the ICU.[24 25] The lower rate of BSIs for midlines in our study may be related to factors such as insertion site, shorter dwell time and higher frequency of antibiotic treatment. In our study, two of four MLABSI cases had a concurrent CVC, which makes the result more difficult to interpret. Minor complications were more common, especially dislodgement of the MC, often leading to premature removal. The minor complications suggest that MCs need to be secured in a better way in the clinical routine. Despite this, 79% of patients were managed without receiving a subsequent CVC during the hospitalisation, indicating that the initial use of MCs could minimise CVC use.

Only 14% of patients were transferred to the ICU, indicating that IMCUs, when organised as in our setting, could potentially relieve ICUs for patients with circulatory failure requiring short-term administration of NE. The in-hospital mortality was 32%, comparable to a large meta-analysis of septic shock in the ICU, displaying a 30-day mortality of 35%.[26] But the populations differ in several aspects, with patients in our study being, on average, 9 years older than in the ICU meta-analysis (73 vs 64 years). In addition, many of the patients had a ceiling of care decision, where full ICU treatment was not considered beneficial, most likely due to age and comorbidities. For this frailer group, IMCUs could enable NE treatment, and we often consider an initial NE trial in the IMCU a better alternative than excessive amounts of fluid resuscitation in a regular hospital ward.[1] Of the 72 who died while in the IMCU, 69 had a documented ceiling of care decision, indicating that unexpected IMCU mortality was infrequent.

Strengths of the current study include a large real-life patient cohort and a prespecified protocol with defined outcomes. The main limitations are associated with the study's retrospective nature with a risk of ascertainment bias; all variables were dependent on documentation within the clinical routine. The registration of vital signs

was sometimes incomplete and as stated above, in some cases NE could have been started in a PVC before baseline, affecting vital signs. For complications, assuming negative results if no complications had been documented in the charts may underestimate true frequencies. Even with the prespecified definitions, interpretation may be necessary as to why any uncertainties were reviewed and discussed in the study group. Interpretation could introduce assessment bias, as all authors were affiliated with the departments included in the study. We tried to minimise this by prespecifying criteria as closely as possible and applying a liberal interpretation for outcomes. For example, in the only extravasation event, the patient did not develop symptoms. Therefore, it did not strictly fulfil our prespecified criteria but was considered an extravasation event in the end, as medical records clearly stated that extravasation was suspected. Additional data on fluid therapy and antibiotics would have helped characterise the population further. The study population was selected by treatment (NE in MC in an IMCU) rather than medical condition (eg, septic shock), which will vary across centres, affecting representativity. Our IMCU population is likely to have a higher degree of frailty than the average ICU population and could be more prone to complications. Finally, our results regarding patient outcomes (eg, ICU transfer) are dependent on the local healthcare organisation, limiting the external validity.

Future studies of vascular devices should ideally report detailed characteristics of the catheter to overcome inconsistencies in nomenclature and facilitate comparisons. Today, the nomenclature is confusing, with many different catheter types being labelled as 'midlines'.[27] In addition, studies of both short-term and long-term outcomes in clearly defined IMCU populations elsewhere are needed to determine for which patients the IMCU is the most appropriate level of care. If future studies show similar outcomes as for ICU care, the IMCU would be preferable, as it is more resource-efficient. This could then enable more patients to receive an appropriate level of care if the caseload of patients with septic shock increases due to the projected demographic change. This could also make vasopressor treatment more accessible in resource-limited settings.

To conclude, the administration of moderate doses of NE in MCs was associated with a low rate of short-term complications and could decrease the need for CVCs. MCs can enable the initial management of circulatory failure in the IMCU, but close monitoring, vigilance and co-operation with intensive care is recommended. More studies are needed to determine the long-term value of IMCU care.

Contributors GT and HH conceived the study, which was designed by GT, MO, VM and HH. Data acquisition was conducted by HK, GT and AA. HK and GT analysed the data and drafted the manuscript, which was critically revised by AA, VM, MO and HH. GT is the study guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Swedish Ethical Review Authority, #2022-06476, consent was waived by the IRB due to the study's retrospective nature.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The data in the current study cannot be publicly shared due to privacy concerns. Researchers may contact the corresponding author with requests for data. Such requests will require IRB approval as well as approval from the data protection officer at Skåne university hospital.

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