

ORIGINAL ARTICLE

Safety of Peripheral Vasoactive Drug Administration in Prehospital and Retrieval Medicine (SPOTLESS-2): A Prospective Observational Cohort Study

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ABSTRACT

Introduction: Adrenaline and noradrenaline are cornerstones of critical care. Traditionally, delivery of these drugs has been through central venous access due to concerns over the safety of peripheral venous access. However, central venous access also may lead to delays and complications, so there is increasing use of peripheral vasoactive drugs. There is evidence for the safety of peripheral administration in controlled theatre and intensive care settings but limited evidence in Prehospital and Retrieval Medicine.

Methods: We conducted a prospective, observational cohort study including patients transferred by Lifeflight Medicine from April 2022 to August 2023. The primary outcome was to establish the safety of peripheral adrenaline and noradrenaline. Patients receiving adrenaline or noradrenaline via peripheral intravenous cannula were included and data on venous access, drug delivery, and complications during transfer was collected. Patients were followed to 24 h post arrival to the receiving facility.

Results: A total of 656 patients were screened, 468 met the inclusion criteria. Patients were predominantly men (60%), median age of 64, 74% of patients were transferred by rotary wing. Noradrenaline was the most common infusion (72%) with a median dose of 0.1 µg/kg/min, and 0.13 µg/kg/min for adrenaline. The anterior cubital fossa was the most common infusion site (78%). Septic shock was the most common indication (47%). The median duration of infusion was 85 min. 93.4% of patients experienced no events with the peripheral infusion; of the remaining 31 patients, 13 (2.8%) had minor technical issues with drug delivery, 14 (3%) had minor complications affecting patient care and 4 (0.8%) required conversion to central access in transit. There were no tissue complications at 24 h follow-up.

Conclusion: Our data suggests that adrenaline and noradrenaline may be safely administered peripherally in Prehospital and Retrieval Medicine environments, with a low overall risk of complications.

Trial Registration: The study was pre-registered on the Australian and New Zealand Clinical Trials Registry (ACTRN12622000404729)

1 | Introduction

Traditional teaching has long cautioned against administering vasoactive agents such as adrenaline and noradrenaline via peripheral intravenous lines due to the risk of tissue injury from extravasation [1–4]. Concerns have also centered on the perceived lack of line security compared with central access, making peripheral infusions more vulnerable to accidental disconnection, interruptions in drug delivery, as well as an increased risk of cannula becoming dislodged from the vein leading to “tissued” lines and potential tissue irritation, pain, or necrosis. This has historically reinforced a preference for central venous administration, despite its procedural complexity and associated risks [5, 6].

Over recent years, this paradigm has been challenged. Peripheral administration is now increasingly used [7–12] either as a bridge while establishing central access or, in selected cases, as the sole route, and mounting evidence supports its safety. Complication rates vary by setting, ranging from as low as 0.035% in surgical theatre [10] to approximately 5% in emergency departments and ICUs [8, 9, 13]. Most adverse events reported were minor and preventable through careful cannula placement, secure fixation, and vigilant monitoring [7, 8].

Uncertainty also persists around optimal drug concentrations for peripheral use. Recent guidelines from the Intensive Care Society recommend a reduced low concentration of 16 µg/mL [14], based largely on expert consensus. While dilute preparations have proven safe [15], evidence is lacking for more concentrated solutions. Our service, Lifelight Medicine (LM), routinely uses concentrations of 60 µg/mL for operational and logistical reasons, making the safety evaluation of these higher doses particularly relevant.

In the prehospital and retrieval medicine (PHRM) environment, delivering vasoactive infusions is especially challenging. The need for rapid hemodynamic support must be weighed against the procedural risk and time cost of central venous catheterization, which carries a mechanical complication rate of 5%–19% [4–6]. Prehospital data, including our own service [7, 16] which retrospectively evaluated 418 patients and reported no major complications and minor complications in 4.7% of cases, are encouraging but remain constrained by small sample sizes and retrospective designs.

The primary outcome of this study was to establish the safety of administering peripheral adrenaline and noradrenaline. This study adds to the literature as the largest and only prospective trial in the PHRM environment and uniquely includes patient follow-up to 24 h.

2 | Methods

2.1 | Study Design

This was a prospective observational study conducted within Lifelight Medicine (LM) PHRM service. The study aimed to evaluate the safety profile of peripheral vasoactive administration, with particular focus on complications occurring up to 24 h after patient retrieval and arrival at destination hospital. Ethics

approval was obtained from the Metro North Health Human Research Ethics Committee (HREC/2022/QRBW/84346) with concurrent Public Health Act approval for 24-h follow-up using “The Viewer.” The study was pre-registered on the Australian and New Zealand Clinical Trials Registry (ACTRN12622000404729). A waiver of consent was granted, acknowledging that the research design and data collection posed no additional risk beyond that expected during the provision of standard emergency medical care delivered by LM and the observational design of the project did not influence the provision of patient care.

2.2 | Setting

LM provides aeromedical services to Queensland, Australia, under the governance and tasking of Retrieval Services Queensland (RSQ). The pre-hospital environment covered is quite unique with a range of terrains, challenging climate and a widely spaced patient population of 5.6 million [17] across 1.7 m Km². LM performs over 8000 missions a year of which around 70% are rotary wing, 20% fixed wing and 5% mixed or road assets based across Queensland. The inherent geography often involves long retrieval times or the use of multiple platforms to facilitate rapid patient transfers from the roadside or rural and regional facilities to major tertiary centers. LM provides both inter-hospital transfers and primary retrievals to Queensland Health (QH) receiving hospitals.

2.3 | Peripheral Vasoactive Administration Protocol

LM uses a standard concentration of adrenaline and noradrenaline for both central and peripheral administration of 3 mg in 50 mL of 0.9% saline, resulting in a concentration of 60 µg/mL. For pediatric patients, a different concentration of 20 µg/mL is used in accordance with the *Children's Health Queensland Child Resuscitation Emergency Drug Dosing (CREDD)* guideline [18].

Infusions are delivered using a B. Braun Perfusor syringe driver with a minimum-volume extension set, attached directly to a valve of a dedicated peripheral cannula. The service guideline specifies a cannula, preferentially placed in a proximal forearm or antecubital fossa vein, and secured with adhesive and transparent semipermeable dressings to minimize dislodgement. Rotary-wing aircraft carry two syringe drivers and one B. Braun Infusomat pump, while fixed-wing aircraft may carry additional equipment.

Patients are suggested to be packaged with cannula sites visible at all times, not in flexion or compression and with linear runs of extension tubing to minimize kinking. All lines are suggested to be inspected at least every 15 min during transport for signs of infiltration or extravasation and infusion continuity is prioritized to minimize interruptions.

2.4 | Eligibility Criteria

Patients were excluded if they met any of the following criteria:

1. Did not receive adrenaline or noradrenaline.

2. Under 16 years old.
3. Vasoactive drug was delivered via a peripheral limb cannula longer than 5 cm.
4. Death at scene or during the first 30 min of the infusion.
5. Transfer to a facility outside Queensland Health, preventing follow-up.
6. Conversion to central venous access prior to departure from the scene or facility.
7. Received push-dose vasoactive drug only.

2.5 | Data Collection

Data capture began on 1 April 2022 and concluded on 31 August 2023, when 625 cases had been logged. A mandatory field was incorporated into the service's electronic AirMaestro database for all missions. If the attending clinician indicated "Yes" to peripheral vasoactive medication use, an automated, study-specific data capture form was generated.

Data capture happens during transfer in two formats—paper based for various clinical aspects and electronic based. Prior to commencement of the study, additional fields were added to the AirMaestro electronic database to enable the collection of specific data points in relation to the provision of peripheral vasoactives. These data points are captured during transfer and entered either during transfer or as soon as practical after; importantly, the data is already captured routinely as part of the provision of care.

Follow-up for complications within 24 h of retrieval was undertaken using "The Viewer", a state-wide Queensland Health electronic patient record which was examined for documented diagnosis of tissue complications or any procedure for tissue management.

2.6 | Data Verification

All logged cases were manually reviewed by AQ, including both electronic and handwritten case sheets, to confirm eligibility. Eligible patients were then followed up in "The Viewer" database for documentation of complications to 24 h post-retrieval. Where data was unclear, RLG provided a second review to reach consensus.

2.7 | Outcome Measures

The primary outcome was the incidence of any complication attributable to peripheral vasoactive administration within 24 h of initiation. Complications were categorized based on their impact on the patient or on delivery of care, as recorded by the attending clinician at the time of data entry:

- In transit technical issues: Minor events noted during treatment that did not affect patient care (e.g., kinking/high-pressure alarm).

- Minor complications: Any event with a measurable effect on the patient's physiological status or clinical course (e.g., labile BP/difficult titration, infiltration/cannula dislodgement).
- Major Complications: Any tissue-related injury or requirement for conversion to central venous access due to failure of the peripheral route during transport.

2.8 | Definitions of Complications

Clinicians were asked to self-report common problems with a simple yes or no box and had the ability to add free text to elaborate on the type or duration of these.

"Line kinking/high-pressure alarm" was defined as transient failure of drug delivery not affecting patient hemodynamics caused by pump alarm stopping delivery for high pressure and/or a kink in the delivery line or cannula which when straightened resolved the alarm.

"Labile blood pressure/difficult titration" was based on the impression of the clinician that the flow of drug delivery was variable and had a resultant impact on the blood pressure requiring alterations to both the lines and cannula position and the rate of vasoactive administration.

"Tissue infiltration" was defined as any skin blanching or pallor around the cannula site or evidence on clinical or ultrasound examination of the area around the cannula suggestive of fluid leak from the cannula into the extravascular space.

"Cannula dislodgement" this was defined as the cannula either coming out of the patient completely or enough the cannula coming out that it was deemed unable to be used safely.

"Tissue-related injury" was defined as any tissue complication beyond skin blanching on the same limb as the delivery cannula. This could include tissue requiring treatment including topical or injected vasodilators or surgical management to aid tissue perfusion or manage tissue compromise.

Secondary outcomes included the type of complications, maximum infusion rates, and the proportion of patients receiving single versus dual vasoactives and overall mortality.

2.9 | Statistical Analysis

Data were analyzed using Microsoft Excel and IBM SPSS Statistics (version 31.0.0.0). Incidence rates and relative risks were calculated to describe the safety profile of peripheral vasoactive use. Mann-Whitney *U* tests were used to compare maximum infusion rates between single- and dual-pressor infusions. Confidence intervals for proportions were calculated in Excel. The test of one proportion was calculated in SPSS using a test value of 0.047 in line with SPOTLESS 1 and defining success as not having experienced a safety event. A Sankey diagram was constructed using [SankeyMATIC.com](https://sankeymatic.com) (Steve Bogart).

TABLE 1 | Case characteristics: Use of peripheral vasopressors.

Characteristic	Noradrenaline <i>n</i> (%)	Adrenaline <i>n</i> (%)	Dual pressor <i>n</i> (%)	Total <i>n</i> (%)
Patient characteristics				
Age (years) <i>m</i> (sd)	60.94 (18.1)	53.9 (21.4)	59.97 (17.2)	59.39 (18.8)
Sex				
Male <i>n</i>	207	58	17	282
Age: <i>m</i> (sd)	62.1 (17.5)	56.9 (19.8)	65.1 (19.1)	61.7 (18.2)
Female <i>n</i>	131	42	12	185
Age: <i>m</i> (sd)	58.9 (18.2)	49.9 (23.0)	52.67 (11.1)	56.5 (19.4)
Transport characteristics				
Transport platform				
Rotary	247 (72.8)	76 (76)	24 (82.7)	437 (74.1)
Fixed wing	58 (17.1)	10 (10)	3 (10.3)	71 (15.1)
Road	29 (8.5)	13 (13)	2 (6.9)	44 (9.4)
Jet	5 (1.4)	1 (1)	0 (0)	6 (1.3)
Transport priority level				
Priority 1 (< 1 h)	109 (32.5)	79 (79)	14 (48.2)	202 (43.1)
Priority 2 (1–3 h)	178 (52.5)	18 (18)	14 (48.2)	210 (44.9)
Priority 3 (3–6 h)	51 (15.0)	2 (2)	1 (3.4)	54 (11.5)
Priority 4 (6–24 h)	1 (0.2)	1 (1)	0 (0)	2 (0.4)
Case characteristics				
Indication ^a				
Other ^b	36 (10.7)	27 (27.2)	1 (3.4)	64 (13.8)
Shock (total)	252 (75.4)	64 (64.6)	28 (96.5)	344 (74.4)
Cardiogenic shock	14 (4.1)	43 (43.43)	3 (10.3)	60 (12.9)
Mixed septic and cardiogenic shock	1 (0.30)	0 (0)	0 (0)	1 (0.2)
Neurogenic shock	1 (0.30)	0 (0)	0 (0)	1 (0.2)
Septic shock	198 (59.2)	7 (7.0)	18 (62.0)	223 (48.2)
Shock unknown cause ^c	38 (11.3)	14 (14.1)	7 (24.1)	59 (12.7)
Toxicology and Envenomation	14 (4.1)	3 (3.0)	0 (0)	17 (3.6)
Trauma	32 (9.5)	5 (5.0)	0 (0)	37 (8.0)

Abbreviations: *m*, mean; *n*, number; sd = standard deviation.

^aThere was six instances of vasopressor use for an unknown indication, one adrenaline and five noradrenaline.

^bOther encompasses anaphylaxis (*n* = 3), haemorrhage (*n* = 8), massive PE (*n* = 1) and other (*n* = 50).

^cThere is no additional information recorded.

3 | Results

3.1 | Patient Cohort

A total of 619 patients were transported during the study period while receiving peripheral vasoactives. Patient characteristics are summarized in Table 1. Overall, recipients were more often male (60.4%) and had a median age of 64 years (IQR 50–73). The predominant indication for peripheral vasoactive use was shock

(*n* = 344; 73.5%), with septic shock accounting for nearly half (*n* = 223; 47.6%).

3.2 | Exclusions and Loss to Follow-Up

Forty cases (6.5%) were excluded due to loss to follow-up. Reasons included: no hospital records located (typically due to private hospital or interstate transfer)—*n* = 24, death at scene or

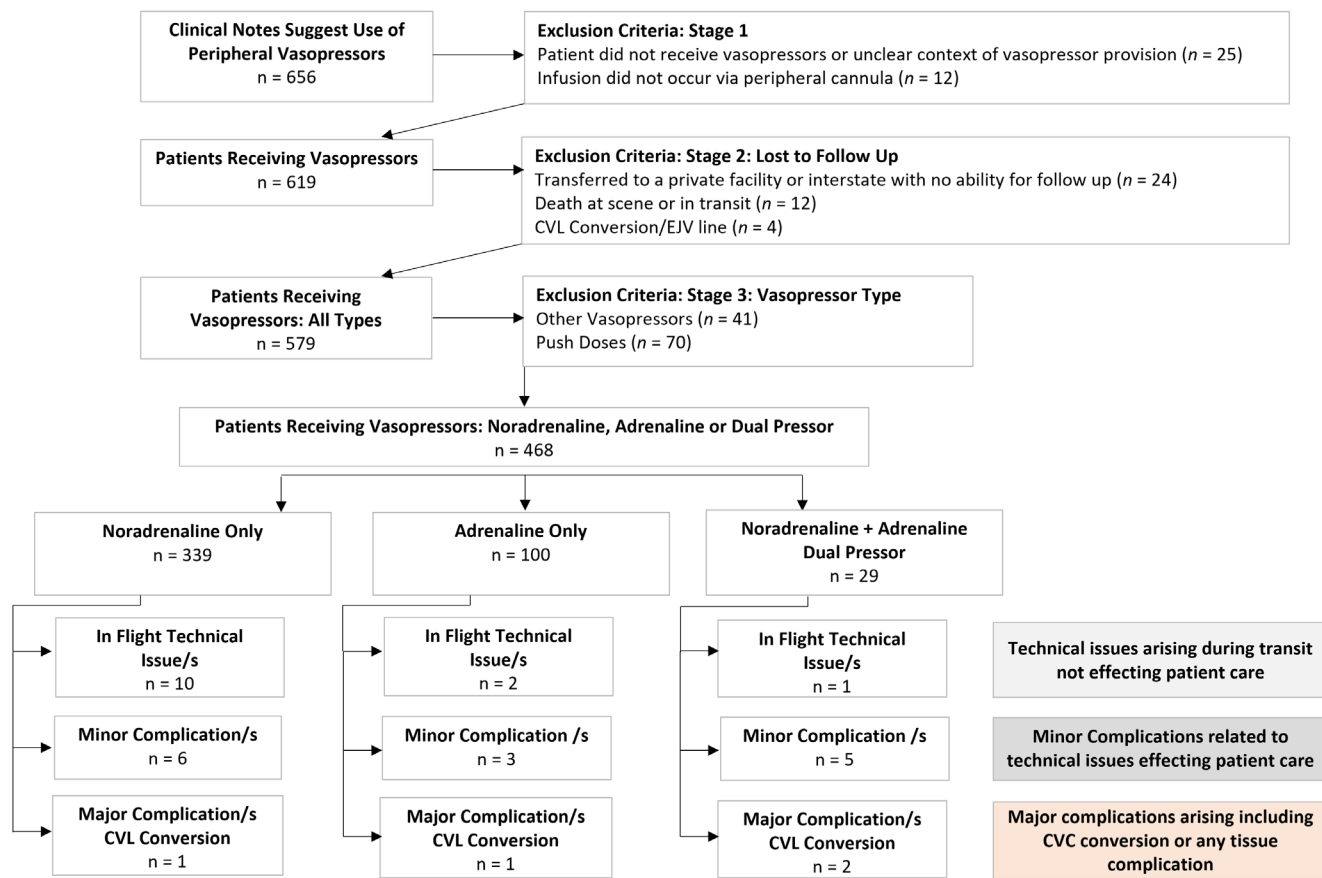


FIGURE 1 | Peripheral vasopressor study inclusion criteria and safety outcomes.

in transit— $n=12$, conversion prior to departure to central venous line or external jugular vein access— $n=4$. An additional 111 cases were excluded due to administration of non-study vasoactives or push doses only. After exclusions, 468 patients were included in the final analysis (Figure 1).

3.3 | Peripheral Vasoactives, Cannula Size and Location

Noradrenaline was the most frequently used peripheral vasoactive ($n=339$; 72.4%), followed by adrenaline and dual pressor combinations. The most common cannulation site was the antecubital fossa (ACF) (78.6% of all infusions). 62% of cannulas were 18 Gauge (G) and 23.6% were 20G. Increasing cannula size was associated with reduced complications 20G 6.25%, 18G 3.17% and 16G 3.7%. ACF cannulas had an increased rate of complication 2.62% compared to non-ACF cannulas 2.15% (Table 2).

3.4 | Infusion Characteristics

Median infusion rates differed by agent and combination (Figures 2 and 3; Table 3). For noradrenaline, the median maximum dose was 9 mic/min ($0.1\mu\text{g}/\text{kg}/\text{min}$) (IQR 5–12 $\mu\text{g}/\text{min}$), compared to 20 $\mu\text{g}/\text{min}$ ($0.13\mu\text{g}/\text{kg}/\text{min}$) (IQR 15–30 $\mu\text{g}/\text{min}$) in dual-pressor use. A Mann–Whitney U test indicated a significantly higher dosage of noradrenaline between the single and

dual pressor use ($U(29, 339) = 7887, p < 0.001$). The median dose for adrenaline was 10 mic/min for both single and dual pressor use (Single use: IQR 6–20; Dual use: IQR 5–20). No significant difference was observed between single vs. dual adrenaline infusion dosing ($p = 0.5$).

3.5 | Safety Events

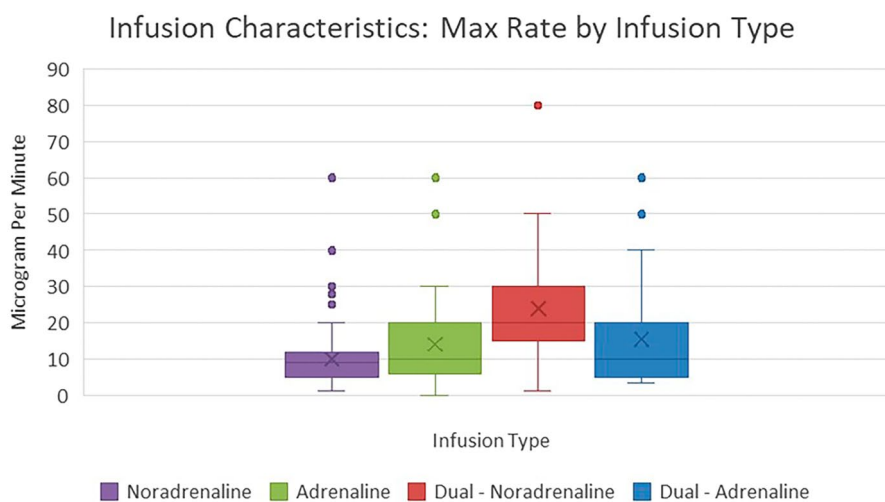
Safety events were recorded in 27 cases, differentiated by 13 in transit technical issues and 14 minor complications (Table 4 and Figure 4). The most common was the in transit technical issue of kinking/high pressure alarm ($n=13$), followed by the most common minor complications of labile BP or difficult titration ($n=10$). Of the minor complications dual pressors had the highest proportion per usage with 17.2% of dual pressor usage sustaining a minor complication. No in-flight adverse events (that is, technical issues or minor complications) were recorded in 441 cases (95% CI: 0.916–0.961).

3.6 | Complications and Mortality

There were 4 major complications, all of which were in transit conversion to central access. On review of these cases, all were converted due to physician preference, not failure of peripheral drug delivery. Average doses of adrenaline and noradrenaline for patients converted to central access were all within the reported IQR for adrenaline and noradrenaline. There were 16 fatalities

TABLE 2 | Complications by cannula features.

Cannula feature	Complication rate (minor and major)	Relative risk (95% CI)
Size of cannula		
20 G	6.25%	1.97 (0.73–5.30)
18 G	3.17%	Reference group
16 G	3.7%	1.17 (0.11–10.21)
Site of cannula (single agent and dual pressors)		
ACF	4.1%	0.82 (0.29–2.31)
Non ACF	5%	Reference group
Site of cannula (single agent only)		
ACF	2.62%	1.22 (0.26–5.75)
Non ACF	2.15%	Reference group

**FIGURE 2** | Peripheral vasopressor infusion characteristics: Max rate by infusion type (X represents the mean and the line denotes the median).

during the 24-h follow-up period but none that can be linked to peripheral vasoactives. Cause of death was derived from recorded discharge data; these were all attributable to the patient's initial pathology. No tissue complications were captured to 24 h (Table 2).

3.7 | Blood Pressure Monitoring

Invasive arterial monitoring was performed in 353 patients (76%), with 24% ($n=85$) inserted by the retrieval team. The most frequent reasons for in-transit arterial line insertion were high-dose vasoactive requirement (34%), clinician preference (22%), long transfer duration (12%) (mean 120 min for patients with invasive monitoring vs. 85 min for those without), and inaccurate non-invasive BP (11%).

3.8 | Push Doses

Just over a quarter of patients ($n=118$; 26.4%) received additional push-dose vasoactives on top of their infusions, most

frequently adrenaline ($n=58$; 49.2%) and metaraminol ($n=57$; 48.3%). Patients on adrenaline more commonly required additional push doses (49%) followed by those on adrenaline and noradrenaline (44%).

4 | Discussion

The present study provides the largest prospective dataset to date on peripheral vasopressor administration in PHRM and uniquely contributes safety data for concentrations up to 60 $\mu\text{g}/\text{mL}$. This work adds both evidence on safety, feasibility, current practice and complication rates across a broad cohort of pathology and settings, to deliver robust evidence to guide clinical practice and inform future guidelines.

While the SPOTLESS trial [7] in the PHRM setting demonstrated the safety of peripheral norepinephrine with low complication rates, these findings extend this with prospective evidence to the prehospital and retrieval medicine (PHRM) environment, and to higher concentrations than typically recommended in ICU

Infusion Characteristics: Max Rate by Weight by Infusion Type

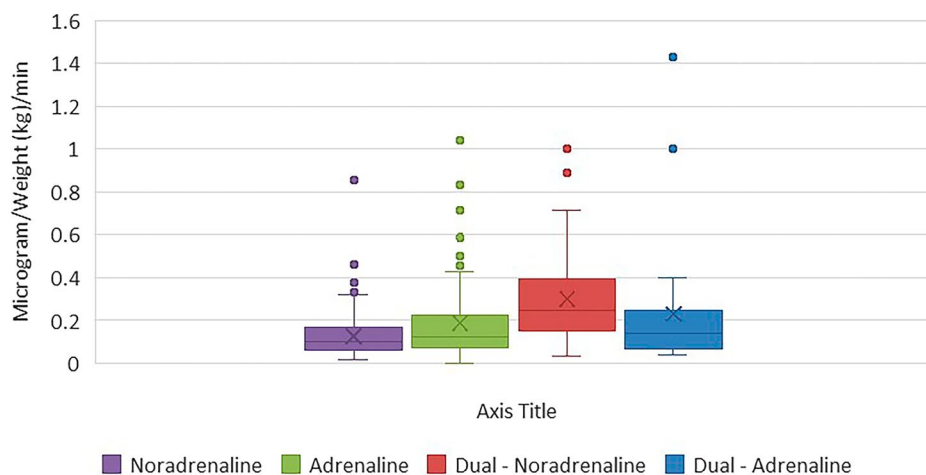


FIGURE 3 | Peripheral vasoactive infusion characteristics: Max rate by weight by infusion type (X represents the mean and the line denotes the median).

guidelines [14]. Combined, these two studies now provide a cohort of over 900 PHRM patients receiving peripheral vasoactives with no major adverse events.

Our initial study [7] informed service guidelines and staff training, standardizing the approach to peripheral vasoactive delivery. In this prospective study involving a large cohort with robust 24-h follow-up, no major tissue complications were recorded despite the high doses and concentrations used. These results provide reassurance that, within a structured and governed system, peripheral vasoactives can be delivered safely in selected patients during transport. They also reinforce the importance of careful patient selection, vigilant monitoring, appropriate packaging, and standardized drug delivery systems.

Our data show that both cannula size and insertion site are associated with complication rates, with larger gauges and non-ACF cannulas having improved safety, echoing ICU literature that highlights the risks associated with sites prone to flexion and compression, such as the antecubital fossa. While the ACF remains a common site in retrieval settings due to access and packaging constraints, these findings support a preference for straighter, less mobile veins where possible. Cannula size also warrants consideration. Smaller-bore devices or sites with compromised flow increase the risk of infusion interruption through pressure alarms or kinking, potentially jeopardizing hemodynamic stability. The retrieval environment imposes unique spatial limitations, but this study emphasizes that patient packaging must facilitate both the protection of cannula position and the ability to visually inspect insertion sites frequently during transport. The frequency of kinking and pressure alarms also relates to the extension tubing delivering the drug from the pump to the cannula. Careful consideration of the path of these lines to ensure they are both straight and visible will reduce the risk of these complications.

The high usage of push dose vasopressors in addition to the peripheral vasoactive infusions highlights both increasing

clinician comfort with push dose vasopressors and a number of practice points. This study captured push dose pressors being administered at any point in LM care of the patient; as a result, some of these may have been while the patient was being stabilized or while waiting for infusions to be drawn up. It does also highlight how unwell this cohort of patients was and how early in their disease trajectory they were. For clinicians, it can inform how to approach and plan for these patients, suggesting that having push dose vasoactives rapidly available, either pre-mixed or drawn up during care is likely to aid in rapid management of our patients despite concurrent infusions.

Decisions regarding central venous access in the acute phase often involve weighing procedural risk, time delays, and the operational cost of performing the intervention in resource-limited or time-critical environments. In our service, central venous access carries a 7%–9% complication or failure rate and substantially increases average scene time. The current data suggest that peripheral administration—at doses and concentrations higher than those in most published literature—offers a safe, rapid alternative for the majority of retrieval patients requiring vasoactive support. These findings support a more selective approach to central line insertion, reserving it for cases where prolonged infusions, high access security, or multiple incompatible infusions are anticipated.

Recent research has underscored the limitations of non-invasive blood pressure monitoring [19, 20], particularly in dynamic transport environments, and has advocated for targeted use of invasive arterial lines. In our cohort, invasive arterial monitoring was used in 76% of cases, reflecting current service practice.

However, introducing additional procedures during retrieval must be balanced against potential delays and operational constraints, particularly in aeromedical missions. Emerging evidence suggests that patients at extremes of blood pressure, or those with rapid hemodynamic fluctuations, may benefit most from invasive monitoring. Our findings highlight the need to

TABLE 3 | Infusion characteristics: Use of peripheral vasopressors.

Infusion characteristics	Noradrenaline,		Adrenaline, Median (IQR)		Dual pressor noradrenaline, Median (IQR)		Dual pressor adrenaline, Median (IQR)		Total, Median (IQR)	
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Median dose (IQR) (Microg/min)	9 (5–12)		10 (6–20)		20 (15–30)		10 (5–20)		10 (5–15)	
Median dose (IQR) (Microg/kg/min)	0.1 (0.063–0.167)		0.13 (0.07–0.222)		0.25 (0.155–0.387)		0.14 (0.065–0.238)		0.11 (0.067–0.181)	
Patient weight	80 (70–100)		80 (69–100)		90 (65–108)		80 (70–100)		80 (70–100)	
Duration, minutes (IQR) ^a	90 (60–160)		53 (27.5–85)		120 (75–150)		60 (17.5–120)		85 (33–135)	
Cannula site	Noradrenaline, n (%)		Adrenaline, n (%)		Dual pressor noradrenaline, n (%)		Dual pressor adrenaline, n (%)		Total^b	
Antecubital fossa	263 (78.0)		80 (80.8)		23 (82.1)		21 (75)		387 (78.6)	
Hand	16 (4.7)		7 (7.0)		2 (7.1)		3 (10.7)		28 (5.6)	
Forearm	44 (13.0)		9 (9.1)		1 (3.6)		1 (3.6)		55 (11.2)	
Upper arm	10 (2.9)		2 (2.0)		1 (3.6)		1 (3.6)		14 (2.8)	
Foot and other	4 (1.1)		1 (1.01)		1 (3.5)		2 (7.1)		8 (1.6)	
Cannula size										
22	2 (0.5)		3 (2.3)		1 (3.5)		1 (3.5)		7 (1.4)	
20	86 (23.6)		20 (15.8)		6 (21.4)		7 (25)		119 (24.3)	
18	226 (62.2)		71 (56.3)		18 (64.2)		17 (60.7)		332 (67.8)	
Less than 18	21 (5.7)		4 (3.1)		3 (10.7)		3 (10.7)		31 (6.3)	
Push dose					Dual pressor n (%)					
Percentage requiring push dose	55 (16.4)		49 (49.4)		13 (44.8)					
Predominate type of push dose	Metaraminol (n=45)		Adrenaline (n=41)		Adrenaline (n=6) and Metaraminol (n=7)					

^aThere are six cases where the infusion duration is not known.

^bTotal includes counts of all cannulas, this includes use of two cannulas for dual pressors.

TABLE 4 | Peripheral vasopressor safety overview: Minor and major complications in flight.

Safety event classification	Noradrenaline	Adrenaline	Dual pressor	Total
Event type	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
In transit technical issues not effecting patient care				
Kinking/High pressure alarm	10 (2.9)	2 (2)	1 (3.4)	13 (2.7)
Minor complications in flight effecting patient care				
Labile BP/difficult titration	4 (1.1)	3 (3)	3 (10.3)	10 (2.1)
Dosing error	1 (0.2)	0 (0)	0 (0)	1 (0.2)
Infiltration	1 (0.2)	0 (0)	0 (0)	1 (0.2)
Infiltration/cannula dislodgement	0 (0)	0 (0)	2 (6.9)	2 (0.4)
Major complications				
CVL conversion	1 (0.2)	1 (1)	2 (6.9)	4 (0.8)
Survival status[†]				
Death during transit	0 (0)	0 (0)	1 (3.4)	1 (0.21)
Death following transit	2 (0.5)	8 (8)	5 (17.2)	15 (3.2)

[†]Death during transit relates to a death over 30min after the team departed the scene/referring facility.

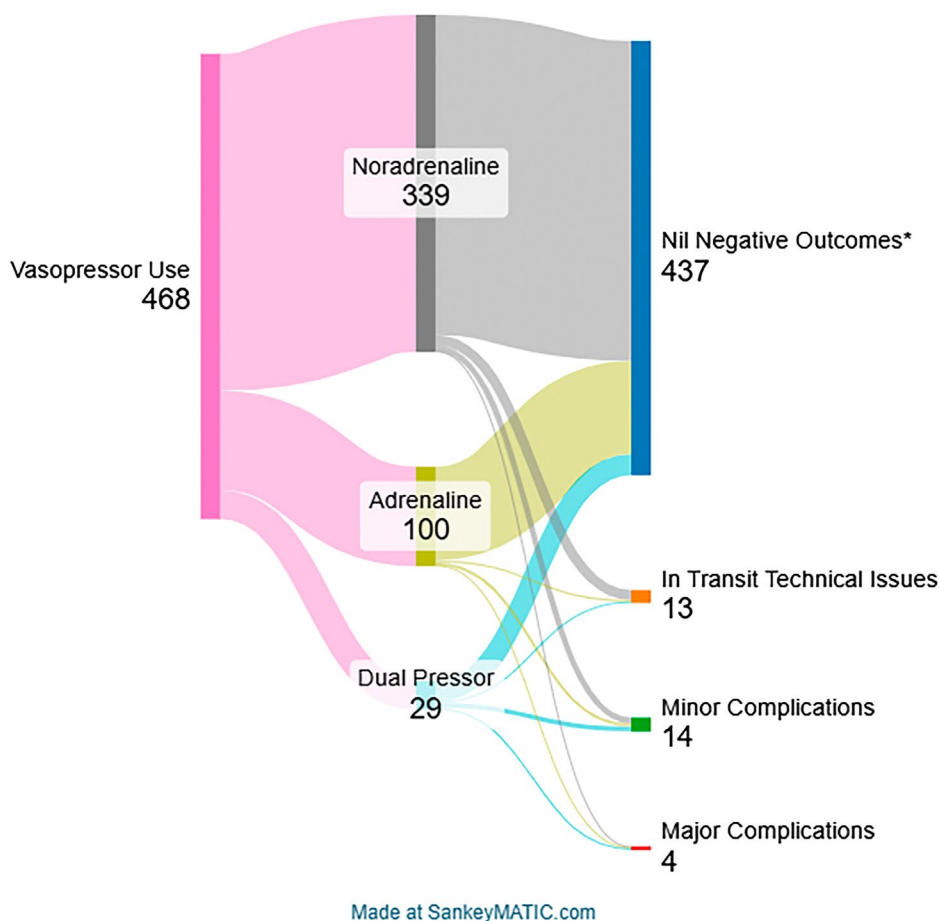


FIGURE 4 | Sankey Diagram *Deaths not attributed to peripheral vasoactive drugs are listed under nil negative outcomes.

integrate patient selection criteria, anticipated clinical trajectory, and transfer duration into decision-making for arterial line placement in the retrieval context.

Given the geography of the area our service covers, transfer times over 1 h are common and patient care can extend for multiple hours including the initial treatment and stabilization carried

out prior to transport. This is generalizable to other remote and rural emergency medical services, although LM's model of care of a senior physician and senior critical care nurse or paramedic with dedicated long-range transfer aircraft and medication may be different from that of many services. We feel the broader message of this data is generalizable to the first hours of many patients' critical care and given our extended care times, in many urban areas, this would span initial Prehospital care into the initial resuscitation in the emergency department. The drug concentrations, dosing, selection and monitoring of peripheral access as well as considerations to minimize technical complications all translate across the broader acute phase of critical care to allow informed treatment decisions for patients.

Our future direction is to incorporate this and other new evidence into our clinical procedures and training to aid clinical decision making for patient selection, vascular access, and monitoring in what has traditionally been an evidence light field.

5 | Limitations

A potential weakness of our study is an inherent selection bias by experienced clinicians of patients felt to be both lower risk and inherently more suitable to receive peripheral vasoactives which may artificially decrease our adverse event rate. We feel that with the dosing being provided and the 3.4% mortality at 24 h after exclusions of early deaths that this data set represents a broad and critically unwell cohort of patients which could be applied to many settings.

The mixture of contemporaneous paper record and electronic record completed after the case means there was potential for some retrospective data change. The cases were all reviewed by AQ and discrepancies were discussed with RLG before resolving them.

Other limitations relate to the difficulty with capturing small tissue events during inpatient follow-up as documentation of minor delivery site issues might be limited and hard to capture.

The dosing of both adrenaline and noradrenaline in our data set is relatively modest, although the spread of dosing presented in Figures 2 and 3 is wide; overall, our data applies to the safety of dosing around 0.6–1.5 µg/kg/min of adrenaline and noradrenaline.

The data we captured is also heavily weighted to noradrenaline, which made up over 70% of our dataset. Given its intramuscular use, adrenaline has less concern for tissue complications, but the 100 cases here will add some further data to that safety profile. Our exclusion of patients initially captured but with no available follow-up does limit capture of potential complications. However, due to the LM governance structure, major complications would still have been reported to LM. LM received no reported complications of peripheral vasoactives in the study period.

6 | Conclusion

In this large prospective cohort of retrieval patients, peripheral administration of adrenaline and noradrenaline—at concentrations up to 60 µg/mL—was delivered without any tissue

complications and with a very low overall complication rate at 24 h. These findings demonstrate that, within a highly trained and governed service, peripheral vasoactives can be safely used as a primary delivery method in selected patients, offering an effective alternative to central venous access. This evidence supports refinement of existing guidelines and encourages a risk-benefit approach to vascular access decisions in time-critical, resource-limited environments.

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Ethics Statement

The study received ethics approval from the Metro North Health Human Research Ethics Committee (HREC/2022/QRBW/84346) with concurrent Public Health Act approval for 24-h follow-up using “The Viewer.”

Consent

Informed consent was waived by the ethics committee for this observational study.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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