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Original Article

A randomised, controlled, feasibility trial comparing vasopressors infused via peripheral cannula versus central venous access for critically ill adults: The VIPCA trial

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ABSTRACT

Objective: To determine the feasibility of conducting a definitive randomised trial to determine whether, in critically ill patients requiring intensive care unit admission, early CVC insertion compared with late CVC insertion leads to increased days-alive-and-out-of-hospital at 30 days (DAH-30) post-treatment.

Design, settings and participants: We conducted a single-centre, parallel-group, feasibility randomised controlled trial with critically ill patients receiving vasopressor infusions randomised in a 1:1 ratio to receive early CVC insertion (within 4 h) or late CVC insertion (after 12 h). All patients received vasopressor infusions via a peripheral intravenous cannula (PIVC) while awaiting CVC insertion. The primary clinical outcome was DAH-30 and the primary feasibility outcome was assessed by evaluating protocol adherence, rates of recruitment, randomisation of eligible patients, retention, follow-up and missing data.

Results: We enrolled 40 patients, 20 patients per group between January 2023 and May 2024. Protocol adherence was significantly lower in the early CVC group (55 %) compared to the late CVC group (100 %, $p < 0.001$). The early CVC group had a median time to CVC insertion of 3.3 h (interquartile range (IQR) 1.2 −3.7 h), within the 4-h target. The early and late CVC groups had a median (IQR) of 13.5 (0.0−23.5) and 19.0 (5.0−23.0) DAH-30 respectively ($P = 0.18$). PIVC complications were similar between the two groups with no severe complications. There were no complications among the 18 CVCs inserted during the trial.

Conclusions: Protocol adherence in the early CVC was much lower than the late CVC. Some protocol modifications will be required to enable the conduct of a larger-scale definitive trial.

Trial Registration: ACTRN12621000721808 (Australia New Zealand Clinical Trials Registry).

1. Introduction

Vasopressor medications, delivered via continuous infusions, are commonly used in critical care environments to restore haemodynamic stability and improve blood pressure in patients with shock states resulting from a variety of aetiologies.[1,2] Common indications for vasopressor infusions encountered in the emergency department (ED) or intensive care unit (ICU) include septic shock,

Abbreviations: CVC, central venous catheter; DAH-30, days alive and out of hospital to day-30; PIVC, peripheral intravenous cannula; ED, emergency department; ICU, intensive care unit; RCT, randomised controlled trial.

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cardiogenic shock, trauma and vasodilatory states due to drug effects (either therapeutic, such as sedatives, or unintentional).

Traditionally, vasopressor infusions are administered via a central vein, which requires the insertion of a central venous catheter (CVC) or some other central venous access device. CVC insertion, however, requires specific expertise, is time-consuming, expensive and associated with a complication rate of up to 15 %.[3] Peripheral intravenous catheters (PIVCs) are quicker to insert, more readily available and have been recommended for administration of vasopressor infusions in patients with contraindications to CVC insertion.[4,5] While there is an increasing body of evidence that administering vasopressor infusions via PIVC may be safe,[6–10] with a low risk of serious complications such as extravasation of vasopressor and tissue injury, recommendations and clinical practice are variable.[11,12]

The only randomised controlled trial (RCT) directly comparing peripheral versus central access in ICU-recruited patients with a broad range of indications for intravenous access, including those without an indication for vasopressor infusion.[13] While it showed a higher rate of complications with PIVC, its design did not provide specific answers regarding the use, specifically prolonged use, of PIVC compared to CVC for the administration of vasopressors.

The aim of the VIPCA trial was to test the feasibility of conducting a definitive, comparative effectiveness RCT to compare the use of PIVC and CVC for the administration of vasopressor infusions for critically ill patients requiring vasopressors in the ED or ICU.

2. Methods

2.1. Design

The VIPCA trial was a single-centre, feasibility, parallel-group RCT. Eligible patients were identified by ED or ICU clinicians or research staff and randomly allocated to a strategy of either early CVC insertion or late CVC insertion for administration of vasopressor infusions. It was conducted within the ED and ICU of a community metropolitan hospital in the state of Queensland, Australia.

The VIPCA feasibility trial was registered with the Australian New Zealand Clinical Trials Registry (Registration number: ACTRN12621000721808) prospectively and is reported here according to widely accepted reporting guidelines for pilot trials.[14] The study protocol was published prior to completion of trial recruitment[15] and is presented in the Electronic Supplementary Material (ESM).

2.2. Ethics and governance

Ethics approval was granted by the Metro North Health Human Research Ethics Committee (HREC/2021/QPCH/74377) with a "consent to continue" model of informed consent. patients were enrolled immediately after being identified as meeting all eligibility criteria. Informed consent was obtained by the treating clinician or research staff *a priori* from the patient if possible. Otherwise, informed consent was obtained at the earliest opportunity once the patient regained the capacity to provide consent. For patients who did not regain the capacity to consent, informed consent was obtained from their substitute decision maker. The ethics committee approved a waiver of consent, where required, for the use of data from enrolled patients who died before consent could be obtained.

An independent data safety monitoring committee (DSMC) comprising of experts in critical care medicine, biostatistics and clinical trials was convened during the protocol development phase and one interim analysis to monitor recruitment, protocol fidelity and safety was performed after the day-30 follow-up was completed for the first 20 patients. The DSMC advised that the trial should continue to completion as planned.

2.3. Study population

Patients were eligible for inclusion in VIPCA if they met all the following criteria:

- Age 18 years or over
- Presented to the ED or admitted to the ICU at the participating hospital
- Deemed to require a vasopressor infusion for any indication by the treating clinician

A vasopressor infusion was defined as the continuous administration of a vasoconstrictor agent (any one of noradrenaline, adrenaline, vasopressin, metaraminol or phenylephrine) via an infusion pump. Single or repeated boluses of vasopressors (such as metaraminol, phenylephrine, and adrenaline) did not constitute a vasopressor infusion.

2.4. Patients were excluded if they

- Were less than 18 years of age,
- Were pregnant (confirmed or suspected),
- Had already received a vasopressor infusion for $\geq$4 h,
- Required >0.1mcg/kg/min of noradrenaline infusion or equivalent (Table S1) at the time of screening,
- Required >1 vasopressor agent,
- Already had a CVC or peripherally inserted central catheter in situ at the time of screening,
- Required CVC insertion for specific therapies (any irritant infusions, parenteral nutrition) other than vasopressors,
- Were deemed to be ineligible for ICU admission or death was deemed to be imminent (i.e., within 24 h) by the treating clinician

2.5. Setting

The VIPCA trial was conducted at an outer metropolitan, general medical-surgical, community hospital state of Queensland, Australia, with 20 acute ED beds, 5 resuscitation beds and 5 ventilator-equivalent ICU beds. It services a population of ~200,000 people. There are approximately 48,000 adult ED presentations and 450 ICU admissions per annum at this hospital.

2.6. Interventions

All included patients received standard medical care as determined by the treating clinician/s, including choice of vasopressors, dosing, titration and weaning. The VIPCA trial only stipulated the route of vasopressor administration by randomising patients to two different timings of CVC insertion. Patients were randomised to either the early or late CVC group.

The early CVC group were treated with early insertion of a CVC for vasopressor infusion. A CVC was to be inserted as soon as practical after randomisation. The target time to CVC insertion and central delivery of vasopressor infusion was $\leq$4 h from randomisation for this group. During the time interval to CVC insertion, patients were treated with vasopressor infusions delivered via a PIVC.

The late CVC group were treated with vasopressor infusions via PIVC, and delayed insertion of a CVC — that is, a CVC was not to be

inserted for at least 12 h from the time of randomisation. PIVCs used for vasopressor infusion were a minimum 20-gauge size (preferably 18-gauge) and inserted in the antecubital fossa or other large peripheral vein. A CVC could be inserted earlier than 12 h for any of the following reasons: need for irritant infusions that cannot be delivered via PIVC, failure of drug delivery via PIVC (due to tissued cannula for example), complications of PIVC (such as drug extravasation or tissue injury), or requirement for noradrenaline infusion or equivalent of ≥0.20mcg/kg/min.

All vasopressor infusion delivery via PIVC in both groups was performed according to the institutional guideline "Peripheral Intravenous Administration of Vasoactive Medication in the Emergency Department" (available in ESM).

Several steps were taken to assist with recruitment rates and protocol adherence. Prior to commencement, and at regular intervals during the recruitment period, trained research coordinators, and ED and ICU investigators, promoted the VIPCA trial and provided staff education at various departmental meetings. Specifically, key aspects of the study protocol, including the inclusion and exclusion criteria, and the details of the two interventions, were discussed with senior medical and nursing staff in both the ED and ICU to ensure that there was support for the conduct of the trial, and that senior clinicians had sufficient clinical equipoise to enable eligible patients to be randomised. Aspects of the inclusion and exclusion criteria, and the two interventions, were regularly highlighted to clinical staff to assist with recruitment and protocol adherence. Patient randomisation packs were available and regularly restocked by research coordinators, in the resuscitation rooms in the ED and at the medical officers' desk in the ICU. When patients were randomised, research coordinators made contact with the treating clinician and discussed the intervention, particularly for patients randomised to the early CVC group. The ED and ICU had a pre-arranged agreement that ICU medical staff would assist with CVC insertion for patients in the early CVC group if ED staff were unable to do so within the 4-h timeframe.

2.7. Outcomes

2.7.1. Feasibility outcomes

The primary outcome was feasibility, defined with the following pre-specified criteria:

- Recruitment rate ≥1 patient per week (1.1 per 1000 adult ED presentations),
- ≥80 % of eligible participants will be randomised
- Protocol fidelity ≥95 % of participants in each of the allocated groups will receive the intervention they were allocated within stipulated timeframes,
- Retention >95 % of patients will consent to ongoing participation in the trial and <10 % of patients will be lost to day-30 follow-up,
- Missing data: <10 %.

2.7.2. Clinical outcomes

The primary clinical outcome was days alive and out of hospital up to day 30 post-randomisation (DAH-30).

Secondary outcomes included, day-30 mortality, hospital length of stay, ICU length of stay, and complications related to line insertions, both CVC and PIVC.

Complications related to CVC and PIVC (local, regional or systemic) during ED and ICU stay:

- Need and reason for replacement
- Extravasation of infused fluid into tissues
- External leakage of infused fluid
- Tissue injury including –
  - Skin erythema/irritation,
  - Skin necrosis,
  - Physician-determined need for phentolamine infiltration,
  - Gangrene or other severe tissue injury requiring surgical intervention
- Central line associated blood stream infection

2.7.3. Process outcomes

Process outcomes included number of PIVC and CVCs inserted and time to insertion of CVC.

A pre-specified sub-study evaluated staff time associated with insertion and monitoring, and factors that influenced clinician choices for PIVC insertion and management of vasopressor infusion.

All data were collected prospectively by trained research coordinators in the ED and ICU. Data was stored on a dedicated RedCap study database.[16,17]

2.8. Sample size

Forty patients were recruited (20 in each group); however, no formal power calculations were performed. This was a feasibility trial and the superiority of one intervention over another was not being tested. This number is within the recommended and observed range for feasibility trials.[18,19] A single pre-specified interim analysis was performed by the DSMC when 20 patients had completed their 30-day follow-up.

2.9. Randomisation

All patients were screened for VIPCA eligibility at the time of vasopressor commencement. Screening logs were maintained in the ED and ICU. All clinical staff in both clinical areas were provided with trial education for the duration of the trial, and were empowered to screen and enrol eligible patients.

Randomisation with allocation concealment was performed using a statistician-generated randomisation sequence and sealed, opaque envelopes. Randomisation was performed using randomised permuted blocks of sizes 2 and 4, and stratified by location, i.e., ED or ICU. Blinding was not feasible, as the presence of a CVC would be readily visible and known to staff, patients and families.

Once randomised, patients were treated according to their treatment allocation as soon as practically possible. Blinding of the staff member performing the follow-up was also not feasible as we did not have funding for a specific blinded individual for this purpose.

2.10. Statistical analysis

The feasibility outcomes were assessed using descriptive statistics against pre-specified benchmarks.

Continuous outcomes were reported as either mean and standard deviation or median and interquartile range, depending on the distribution. Categorical outcomes have been presented as frequency and percentages. The primary clinical outcome of DAH-30 was compared between the groups using median regression and reported as median difference (95 % confidence interval, CI). Secondary outcomes measured using continuous data were compared between groups using median regression. For categorical outcomes, unadjusted risk ratios with 95 % CIs were calculated.

2.11. Funding sources

The VIPCA trial was funded by competitive grants received from The Common Good Foundation (Grant Number: CKW2022-02), Emergency Medicine Foundation (Grant Number: EMJS-411R372022-HOLLAND) and The University of Queensland Mayne Academy of Critical Care Pilot Study Grant. Funding bodies did not have any role in the study design, conduct, analysis or interpretation of findings.

3. Results

3.1. Patient characteristics

There were 40 patients enrolled between January 2023 and May 2024, 20 (50 %) each in the early and late CVC groups, with the final patient follow-up occurring in June 2024. Recruitment details are presented in the flowchart in Fig. 1. There were no losses to follow-up apart from one patient who withdrew consent for the day-30 follow-up, though they provided consent for data already collected during the hospital stay to be used.

Baseline characteristics are presented in Table 1 and Supplementary Table S2. Demographic characteristics, admission reasons and comorbidities were broadly similar. Participants in the early CVC group had a lower arterial pH at admission (median 7.29, IQR 7.24–7.36, compared to 7.37, IQR 7.31–7.41). There were also numerically more patients who received mechanical ventilation (7/20, 35 %, compared to 3/20, 15 %) and renal replacement therapy (2/20, 10 % compared to 0/20, 0 %).

3.2. Feasibility

The overall protocol adherence in the VIPCA trial was 78 % (31/40). The target protocol adherence rate of 95 % was not achieved. Protocol adherence was significantly lower in the early CVC group (11/20, 55 %) compared to the late CVC group (20/20, 100 %, $p < 0.001$). Eleven out of 20 participants (55 %) in the early CVC group underwent CVC insertion within the 4-h target, while one more patient had a CVC inserted after the 4-h mark and the other eight patients (40 %) did not receive a CVC at all. All 20 patients in the late CVC received treatment as per the protocol. Four out of 20 patients (20 %) required CVC insertion and all four CVCs were inserted as per the study protocol, two due to requiring vasopressor infusion after the 12-h mark, and two within 12 h for reason/s specified within the protocol.

The recruitment rate was 0.66 patients per 1000 adult ED presentations (0.61 patients per week). The target recruitment rate of 1 patient per week was not achieved. The total number of patients screened was 97 patients, of which 87 (90 %) were eligible for randomisation. Four eligible patients required urgent transfer to another hospital for services not available at the study hospital. Thus, the final randomisation-to-eligibility percentage was 48 % (40/83). The randomisation-to-screening percentage was 41 % (40/97), or approximately four patients randomised for every ten screened.

The final follow-up rate of 95 % was consistent with our target rate of 95 %. There was no missing data for any of the demographic, treatment, complications or outcomes data, except for missing outcome data for the one patient who withdrew consent for follow-up.

3.3. Treatment

The number of PIVCs and CVCs inserted are detailed in Table 2. There were a similar number of PIVCs in both groups (median 2.5, IQR 2–3.5 vs 3, IQR 2–4 in early and late CVC groups). There were 14 CVCs inserted in 12 patients in the early CVC group and 4 CVCs inserted in 4 patients in the late CVC group. The median time to CVC insertion from randomisation (for patients who received a CVC) was

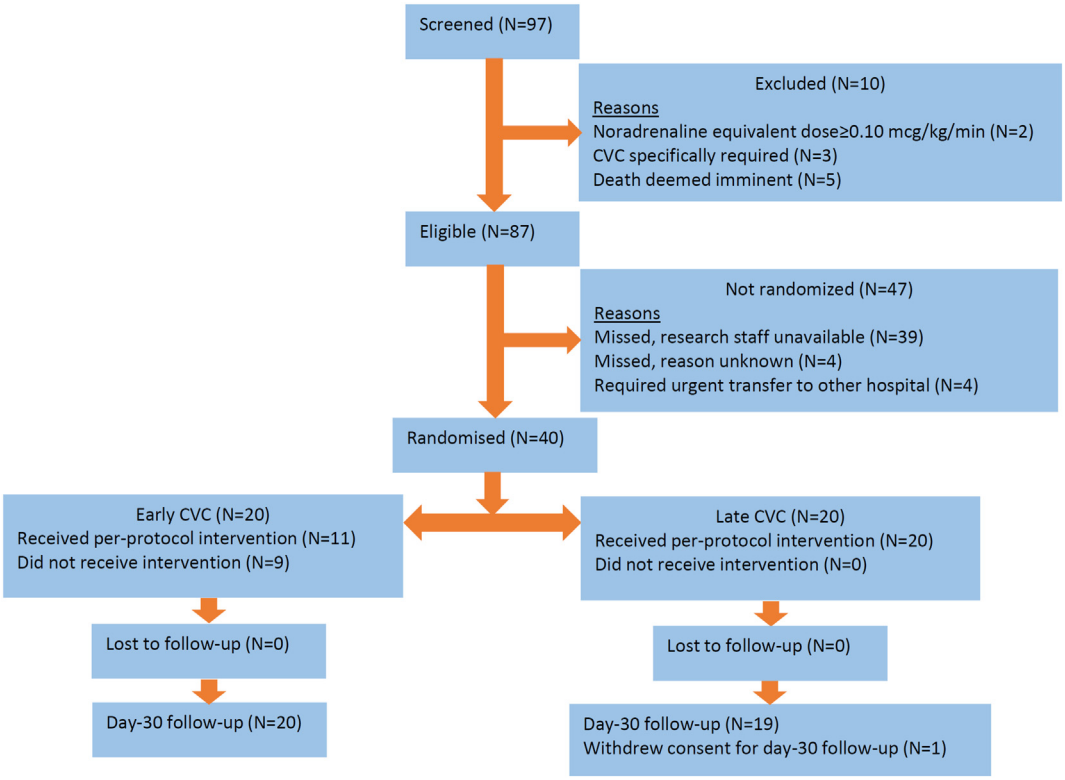

Fig. 1. Recruitment flowchart. "Per-protocol intervention" refers to patients being managed as per their group allocation. Patients in the early CVC group were to have CVC inserted within 4 h. Patients in the late CVC group were not to have CVC inserted for at least 12 h, except under certain circumstances as described in the study interventions.

Table 1
Baseline characteristics for patients allocated to early CVC and late CVC groups.

		Early CVC	Late CVC
		N = 20	N = 20
Age (years)		67.6 (58.7–77.3)	61.7 (57.1–79.8)
Male Sex		11 (55 %)	9 (45 %)
Body mass index		27.9 (26.6–32.1)	25.3 (22.6–28.4)
Sepsis diagnosis		15 (75 %)	16 (80 %)
Site of sepsis	Pulmonary	6 (40 %)	7 (44 %)
	Gastrointestinal	3 (20 %)	2 (13 %)
	Urogenital	4 (27 %)	2 (13 %)
	Central nervous system	1 (7 %)	0 (0 %)
	Endocarditis	1 (7 %)	3 (19 %)
	Skin/soft tissue	0 (0 %)	2 (13 %)
Diabetes		4 (20 %)	2 (10 %)
Hypertension		8 (40 %)	7 (35 %)
IHD		5 (25 %)	4 (20 %)
COPD		3 (15 %)	4 (20 %)
Clinical Frailty Score		4 (3–4.5)	4 (3–6)
Mechanically ventilated		7 (37 %)	3 (16 %)
Renal replacement therapy		2 (11 %)	0 (0 %)
Admission laboratory values			
Arterial pH		7.29 (7.235–7.355)	7.37 (7.31–7.41)
Serum bicarbonate (mmol/L)		22.5 (20.5–24.5)	23 (19–27)
Serum lactate (mmol/L)		2.1 (1–2.95)	1.6 (0.9–3.2)
PaO2/FiO2 ratio		198 (83.3–266)	220 (114 - 390)

Data are presented as median (IQR) for continuous measures, and n (%) for categorical measures. CVC: central venous catheter; IHD: ischaemic heart disease; COPD: chronic obstructive pulmonary disease.

Table 2
Trial processes.

	Early CVC	Late CVC	Effect estimate[a] (95 % CI)	p-value
	N = 20	N = 20		
Protocol adherence	11 (55 %)	20 (100 %)	1.82 (1.22–2.70)	<0.001
Number of PIVCs	2.5 (2–3.5)	3 (2–4)	0 (−1.13 to 1.13)	1
CVC inserted	12 (60 %)	4 (20 %)	0.33 (0.13–0.86)	0.01
Number of CVCs	1 (0–1)	0 (0–0)	−1 (−1.28 to −0.72)	<0.001
Time to CVC insertion (hours)	3.3 (1.2–3.7)	12.2 (7.6–14.7)	8.03 (3.08–12.99)	0.004
Duration of vasopressor infusions (hours)	13 (5.5–36)	11.5 (6.5–23.5)	−7 (−24 to 10)	0.41

CVC: central venous catheter; PIVC: peripheral intravenous cannula.
[a] For continuous variables, univariable median regression was performed with group allocation as the only explanatory variable. For protocol adherence, risk ratio was calculated with 95 % confidence intervals.

3.3 h (IQR 1.2–3.7) in the early CVC group, within our pre-specified target of 4 h. The median duration of vasopressor infusion was similar between the two groups (13 h, IQR 5.5–36 vs 11.5 h, IQR 6.5–23.5 in the early and late CVC groups). All patients received noradrenaline as the initial vasopressor agent in both groups. A total of seven patients required additional vasopressors, with one each receiving adrenaline and vasopressin, and five receiving both adrenaline and vasopressin (Supplementary Table S3).

3.4. Outcomes

The primary clinical outcome, DAH-30, was available for all consenting patients (39/40, 98 %). The early CVC group had a median of 13.5 days (IQR 0–23.5) alive and out of hospital on day 30, while the late CVC group had 19 days (IQR 5–23). The median difference in DAH-30 was 8 days (95 % CI -3.9 to 19.9, p = 0.18). Of note, the distribution of DAH-30 was bimodal (Supplementary Fig. S1). The ICU and hospital lengths of stay were similar between the two groups as detailed in Table 3 and Supplementary Figs. S2 and S3. Day-30 mortality was 3/20 (15 %) in the early CVC group and 1/20 (5 %) in the late CVC group (risk ratio = 0.35, 95 % CI 0.04–3.09, p = 0.32).

3.5. Complications

The overall PIVC complication rate was 20 % (8/40) (Table 4). Of these eight, four (50 %) were issued PIVCs that needed replacement, two (25 %) PIVCs had external leakage and one (13 %) had extravasation with no tissue injury. There were no serious complications such as tissue necrosis, tissue ischaemia, tissue loss or need for surgical or other invasive treatment of any PIVC complications. The PIVC complications were distributed similarly between the two groups. There were no complications among the 18 CVCs inserted.

4. Discussion

4.1. Key findings

Our findings demonstrate that protocol adherence was markedly different between the early CVC and late CVC groups, suggesting there may be significant equipoise issues that influence the timing of critical care clinicians' choice to insert CVCs for the provision of vasopressor infusions. Overall recruitment rates and recruitment of eligible patients were both lower than the pre-specified targets. Some modifications will be required to the VIPCA protocol to enable the successful conduct of a larger trial.

4.2. Feasibility

The retention and follow-up rates were very high and there was no missing data for key study elements. The overall speed of recruitment and randomisation:eligibility ratio was lower than

Table 3
Patient outcomes.

		Early CVC	Late CVC	Effect estimate[b] (95 % CI)	p-value
		N = 20	N = 19[a]		
DAH-30	Median (IQR)	13.5 (0–23.5)	19 (5–23)	8 (−3.9 to 19.9)	0.18
ICU LOS	Median (IQR)	2 (1–4)	3.5 (2–5)	1 (−0.7 to 2.7)	0.24
Hospital LOS	Median (IQR)	7 (4–31)	9 (6–13)	4 (−7.5 to 15.5)	0.49
Day-30 mortality		3 (15 %)	1 (5 %)	0.35 (0.04–3.09)	0.32

CVC: central venous catheter; DAH-30: days alive and out of hospital to day-30; ICU: intensive care unit; LOS: length of stay in days.
[a] 1 patient declined consent for follow-up.
[b] For continuous variables, univariable median regression was performed, as the distribution of the continuous outcomes was highly skewed, with group allocation as the only explanatory variable. For day-30 mortality, risk ratio was calculated with 95 % confidence intervals.

Table 4
Line complications.

	Early CVC	Late CVC	Risk ratio (95 % CI)	p-value
	N = 20	N = 20		
PIVC				
Any complication	4 (20 %)	4 (20 %)	1.00 (0.28–3.45)	1.00
Tissued PIVC	2 (10 %)	2 (10 %)	1.00 (0.16–6.42)	1.00
External leakage	1 (5 %)	1 (5 %)	1.00 (0.07–14.90)	1.00
Extravasation	0 (0 %)	1 (5 %)	–	–
Skin erythema	0 (0 %)	0 (0 %)	–	–
Necrosis/Tissue ischaemia/Loss	0 (0 %)	0 (0 %)	–	–
Other	1 (5 %)	0 (5 %)	-	-
CVC				
Any complication	0 (0 %)	0 (0 %)	–	–
Bleeding	0 (0 %)	0 (0 %)	–	–
Pneumothorax	0 (0 %)	0 (0 %)	–	–
Blocked lumen	0 (0 %)	0 (0 %)	–	–
CLABSI	0 (0 %)	0 (0 %)	–	–
Extravasation	0 (0 %)	0 (0 %)	–	–
Malpositioned line	0 (0 %)	0 (0 %)	–	–
Other	0 (0 %)	0 (0 %)	–	–

Data are presented as n (%).
PIVC: peripheral intravenous cannula; CVC: central venous catheter; CLABSI: central line associated bloodstream infection.

forecast based on observational data, a common finding in the critical care literature,[20] suggesting the need for a multicentre design to achieve appropriate recruitment of a subsequent comparative effectiveness trial. Protocol adherence in the early CVC group was low, suggesting that modifications to the study methodology would be required even if a larger sample could be recruited with a multicentre design and a longer recruitment period. Potential solutions could include the conduct of a trial using dedicated specialised vascular access teams[21] who may be better placed to rapidly insert CVCs than ED or ICU clinicians, a more flexible protocol that allows up to 6–8 h to insert a CVC in the early group, restricting to daylight hours recruitment when staffing levels are generally higher, and a dedicated staff education program throughout the duration of recruitment.

4.3. Implications of findings

There has been mounting observational evidence in recent times suggesting that vasopressor infusions can be delivered safely via PIVCs.[4–7,22] Thus, it was not surprising that most of the patients in the late CVC group were managed with PIVCs, and only select patients received a CVC. The corollary of this was that just over half of the patients randomised to early CVC actually received an early CVC. The remaining patients in that group were managed with vasopressors via PIVC only. This is likely reflective of clinician comfort with a peripheral infusion of vasopressors and lack of equipoise to insert an early CVC in our institution. Any future trial would need to determine local institutional and clinician practices to identify suitable locations where there was sufficient equipoise to conduct such a clinical trial.[23]

Our findings raise the question “Is a CVC always necessary for vasopressor infusions for critically ill patients?”. The VIPCA trial was not powered to answer this question with patient-centred outcomes. While our results may suggest that clinical outcomes could be similar between the two groups, this would need to be demonstrated in a larger trial adequately powered to detect differences in clinical and patient-relevant outcomes. It is likely that such a trial would have a non-inferiority design as there is currently no reason to hypothesise that one or the other method of vasopressor delivery would result in superior outcomes. Findings from such a trial could be practice-changing and result in fewer CVCs being inserted for the purpose of delivering vasopressor infusions. Avoidance of CVC could be a meaningful, patient-important, potential secondary outcome in such a trial.

The complication rates of PIVCs were low, and there were no CVC complications. With regards to CVC, it is likely that there were too few CVCs in this study to make any definitive comments. Furthermore, there is a vast amount of literature describing the risks associated with CVC insertion and maintenance.[3,24] For PIVC, the rate of complications was higher than reported in the literature,[25] but this would be expected given that VIPCA was a randomised trial with dedicated, prospective monitoring of complications, rather than a reliance on retrospective chart review. The complications we observed were minor and did not have any significant consequences for the patients, reiterating the safety of peripherally administered vasopressors.

4.4. Limitations

There are several limitations to consider. As a single-centre study, our findings will undoubtedly be influenced by contextual

factors such as institutional preferences and case mix, and cannot be considered broadly generalisable until replicated in a multicentre trial. The trial was designed for feasibility purposes and thus numbers were small when considering clinical outcomes, and findings should be interpreted cautiously. Less common and rare, but significant, complications cannot be excluded. The adherence to the early CVC strategy was low. It is possible that the true complication rate and outcomes with this strategy were quite different to what was observed and reported, because nearly half the patients in this group did not receive an early CVC. Findings may be different if this trial were conducted at a large tertiary institution with a more established research infrastructure.

5. Conclusion

This study showed that modifications to the current protocol would be required to ensure viability of a larger RCT, particularly with regards to recruitment rates and protocol adherence. A larger, multicentre trial powered to detect differences in clinically meaningful outcomes is necessary to overcome the limitations of a feasibility trial and answer the question of whether early CVC insertion is necessary for all vasopressor infusions for critically ill patients.

CRediT authorship contribution statement

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Consent to participate

Informed consent was obtained from all participants or their legally authorised representative.

Ethics approval

Ethics approval was granted by The Prince Charles Hospital Human Research Ethics Committee (HREC/2021/QPCH/74377).

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Conflict of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Mahesh Ramanan reports financial support was provided by The Common Good Foundation. Thomas Holland reports financial support was provided by Emergency Medicine Foundation. Yogesh Apte reports financial support was provided by The University of Queensland. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Availability of data and material

Deidentified data can be made available for sharing. To request data, please contact the corresponding author with a request. This will be reviewed by the trial management committee. Applications from investigators with suitable academic capability to conduct the proposed work will be considered. Approval from the ethics committee which approved the conduct of this trial will be required prior to sharing of any patient data. If a proposal is approved by the management committee and the ethics committee, a signed data transfer agreement will be required before data sharing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ccrj.2025.100106.

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