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RAPID REVIEW

TRANSFUSION

Peripheral blood stem cell collection: Are midline catheters a viable alternative to central venous catheters?

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Abstract

Background: Vascular access is a rate-limiting step for peripheral blood stem cell collection. In the absence of readily accessible superficial veins, placement of tunnelled or non-tunnelled central venous catheters (CVCs) is common. These invasive access routes create medical risks for patients and are associated with logistical challenges, thus prompting a search for alternatives. One such option is the off-label use of midline catheters.

Study design and methods: We carried out a literature search for published experience with the use of midline catheters for peripheral blood stem cell collection. Data extracted included whether collections were allogeneic or autologous, donor sex, age and weight, inlet flow rate, total blood volumes (TBV) processed, collection duration, number of collections per donor, and achievement of collection targets.

Results: The search produced three reports (one in abstract form) comprising 19 patients and 26 collection events. Donor sex and status were provided for 18 patients; 10 were female, 8 were male, 12 were allogeneic, and 6 autologous. Median (range) for: donor age was 28 (12–59); donor body weight (kg) was 77.5 (45.4–113.4); inlet flow rate (in mL/min) was 66 (28–80); TBV processed (in mL) was 15,880 (6178–21,871); collection duration (in hours) was 5.0 (3.2–7.0); and CD34 × 106/kg collection yield was 5.9 (3.6–23.0). Target CD34 yields were achieved in 14/19 (74%) of donors with 7/19 (37%) requiring two collections days.

Discussion: Peripheral blood stem cell collection does appear to be viable via midline-based catheter access, particularly for allogeneic donors and shorter collection courses. Development of institution-specific guidelines and care pathways are recommended.

KEYWORDS

cellular therapy, transplantation – stem cell

1 | INTRODUCTION

Vascular access is a rate-limiting step for peripheral blood stem cell collection. In the absence of readily accessible superficial veins, placement of tunneled or non-tunneled central venous catheters (CVCs) is common. These

Abbreviations: CVC, central venous catheter; HPC(A), hematopoietic progenitor cell apheresis; MNC(A), mononuclear cell collection apheresis; PICC, peripherally inserted central catheter; r-TPA, recombinant tissue plasminogen activator; SD, standard deviation; TBV, total blood volume.

TABLE 1 Challenges associated with CVC Access.

Logistical issues associated with line placement:
Catheter placed by a proceduralist, whose availability may be limited. This is particularly an issue for unscheduled placement.[a] Specially trained individual required for subsequent removal of CVC.
For internal jugular placement (preferred site) of temporary catheter, post-placement chest radiography required to exclude complications and confirm tip position. If tip within the right atrium, additional time needed to retract the catheter tip.
Medical issues associated with CVC placement and CVC utilization:
Bleeding, hematoma, infection, thrombosis, pneumothorax are recognized complications.
Catheter occlusion may require instillation of r-TPA which could delay procedure start.

[a]In the event, for instance, that superficial vein access is either unsuccessful or becomes untenable during the procedure.

invasive access routes create medical risks for patients and are associated with logistical challenges (see Table 1) prompting a search for alternatives. One such example is placement of needles into deeper superficial veins under ultrasound guidance.[1]

Another option, and the subject of this commentary, is the off-label use of midline catheters. The latter can be supported at many centers via a dedicated nurse-led access team, who are experienced and certified in the use of ultrasound in placement of access devices – such as peripherally inserted central catheters (PICC Lines), midlines, and others. Because midline catheters, which are placed in either the basilic, cephalic or brachial veins and terminate distally to the axillary vein, are considered peripheral intravenous catheters—a post-placement chest x ray is not required for confirmation of placement and specialized training is not required for their removal. The convenience and noninvasiveness of this option makes it attractive for further consideration.

2 | METHODS AND FINDINGS

The literature was therefore reviewed to identify published reports of midline catheters used for HPC-A or MNC-A collection. The search produced 3 reports (1 in abstract form providing limited detail) and comprising a total of 19 patients and 26 collection events (i.e., 1.4 collections per donor). Table 2 provides summary detail. Median (range) age was 28 (12–59) and among the 18 donors in whom sex was reported, there were 10 females and 8 males. The ratio of allogeneic to autologous donors was 2:1 (12 allogeneic and 6 autologous donors among the 18 for whom this data was reported).

Collections 1–17[2] were performed using either a 4 Fr (6 cm) or 5 Fr (8 cm) PowerWand XL (ICU Medical, San Clemente, CA). Most involved bilateral placements to accommodate inlet and return access, but in some cases a single midline was used for inlet and an available superficial vein for the return. In collections 18–25,[3] an unspecified, 5 Fr midline catheter was used with length adjusted to 8–12 cm; 8 collections were performed on 6 donors. Bilateral midlines were placed in 2/6, inlet via left arm PICC line with return via right midline in 2/6, and in the remaining 2/6 a single midline was placed with a peripheral vein used for the remaining access. Quantitative performance data was not provided for collection 26.[4]

Collections 18–25 proceeded at slower rates than collections 1/17; median mL/min (range) of 35 (28–35) versus 70 (50–80), respectively. In addition, collections 18–25 consisted of a much lower total blood volume processed compared to collections 1–17; median mL (range) of 7628 (6178–10,393) versus 17,357 (13,404–21,871), respectively. Both centers performed collections using the Spectra Optia (Terumo BCT, Lakewood, CO). Differences in flow rates may potentially have been accounted for by greater use of bilateral midline catheters in collections 1–17 as well as larger kilogram (kg) body weight of donors of 1–17 compared to 18–25 at median (range) 78.2 kg (45.5–113.4) versus 58 kg (56–87), respectively.

Midline-based collections achieved target CD34 yields in 14/19 (74%) donors; with 7 donors requiring 2 consecutive collection days. Mean CD34 $\times 10^6$/kg (range) yield among 24 HPC(A) collections was 5.6 $\times 10^6$/kg (3.9–23.0). In two patients, increased access pressure in the midline catheter was observed. This was addressed by 1 cm retraction of the catheter away from a venous valve, thus decreasing access pressure.[2] Another donor developed ecchymosis at the insertion site, which resolved within a week.[2]

3 | DISCUSSION AND CONCLUSIONS

Weaknesses of the reported literature includes small overall sample size, under-representation of recipient kilogram body weight (i.e., Casacchia et al., a pediatric transplant center), and mostly single-procedure collections as there was a maximum of 2 collection days in only 7/19 (37%) of donors. For this latter issue, additional experience with midlines is required for patients declaring as poor mobilizers—who often require twice this number of collection days.[5] Additional collection days

TABLE 2 Review of the literature on midline use in cellular therapy collections; collections 1–17: Casacchia et al.; 18–25: Caime et al.; 26: Oleari et al.

Author	Collection	Unique donor	Donor age	Kg	Inlet flow rate (mL/min)	TBV processed (mL)	Collection duration (hours)	CD34 × 10^6/kg	
								Target	Actual
Casacchia	1	1	12	98.0	71	17,601	5.00	5	3.9
	2	2	14	100.0	70	14,983	4.00	5	10.56
	3				70	15,880	6.00		
	4	3	49	78.2	75	16,419	7.00	10	11.1
	5				60	14,000	6.00		
	6	4	13	70.2	70	16,921	5.00	10	14.2
	7	5	59	102.8	75	19,594	6.00	5	5.9
	8				80	20,000	5.00		
	9	6	18	80.2	75	16,287	5.00	15	23
	10	7	12	45.4	66	21,871	7.00	5	5
	11				66	21,112	6.00		
	12	8	51	92.0	70	13,404	5.00	5	7.3
	13	9	19	77.5	50	14,500	5.50	5	4.8
	14	10	14	113.4	67	19,237	5.50	5	8.7
	15	11	20	63.1	70	17,357	5.00	(MNC-A)	(MNC-A)
	16	12	18	51.6	60	17,765	5.25	3.5–5	3.6
	17				60	17,636	5.00		
Caime	18	13	28	61.0	35	10,275	5.32	4–6	9.7
	19	14	41	57	35	7621	3.97	4–6	4.3
	20	15	38	87	35	6178	3.22	4–6	7.1
	21	16	29	56	35	7361	4.12	5	5.0
	22				35	6362	3.57		
	23	17	50	85	35	10,393	4.90	7	5.1
	24	18	44	58	28	7764	4.05	5.0	4.6
	25				28	7634	3.98		
Oleari	26	19	NR	NR	NR	NR	"a few hours"	NR	"adequate"
Median (range)			28 (12–59)	77.5 (45.4–113.4)	66 (28–80)	15,880 (6178–21,871)	5.0 (3.2–7.0)	5.0 (5.0–15.0)	5.9 (3.6–23.0)

Abbreviation: NR, not reported.

may also be required for allogeneic donations where a significant weight discrepancy exists between donor and recipient.

The reported literature of midlines for HPC(A) collection is mostly comprised of adult (or at least, adult-sized) donors—only 1/18 (6%) weighed <50 kg. Selection criteria for midline placement requires sonographic evaluation of the arm veins, assessing for the absence of stenosis, thrombosis, and appropriate vessel diameter. Specifically, a desired catheter-to-vessel ratio of <45% is recommended.[6] A 4 or 5 Fr midline will have an external diameter of ~1.33 to 1.67 mm, respectively. Using the catheter-to-vessel rule, this would require a vessel diameter of at least 2.96 mm.

This perhaps explains the enrichment of Casacchia's midline donor population for larger individuals (particularly given they are a pediatric transplant center). In studies, mean basilic vein diameter ranged from 4.4 mm (±SD 1.4) to 5.1 mm (±SD 1.3 mm)[7,8] among healthy adults, whereas mean upper arm cephalic vein diameter was 2.4 mm (±SD 1.3 mm) among an adult vascular patient population.[9]

In our adult transplant program, overall catheter utilization rate is 50%. Our usual collection flow rates (mL/min) and total blood volume processed (in mL) are 55–65, and 15,000 to 20,000, respectively, thus closely mirroring the collection characteristics reported in Casacchia et al. In contrast, our allogeneic to autologous donor

ratio is 0.5. This differs significantly from midline catheter cohorts represented in the literature with ratios of 1:1 in Caime et al., and 2:1 in Casacchia et al.

As opposed to allogeneic donors, autologous donors tend to have poorer vascular health and sometimes arrive for collection with PICC lines already in place; raising concern that fewer of our autologous donors might therefore be candidates for midline-based collections. At our center, in contrast to Caime et al., we do not view PICC lines to be apheresis competent devices. In support of this, Caime et al. reported median flow rates and total blood volumes processed that were less than half compared to both ours and Casacchia's.

Compared to CVCs, midline catheters have lower risks of catheter related blood stream infection and thrombosis; the risk of thrombophlebitis is lower compared to peripheral catheters.[10] Cited rates for midlines include those of infection: 0.0%–0.3%; phlebitis: 0.3%–1.7%; infiltration or extravasation: 3.5%–10%; and occlusion: 2.6%–17.0%.[11,12] Other risks associated with midlines include erythema at the insertion site, bleeding, and pain.[13] These complications are spread over an average dwell time for midline catheters of 7.7–16.7 days,[10] which is longer than needed for stem cell collection.[5] For example, at our center 73% of all collections (including autologous and allogeneic) are completed within 2 days and 89% within 3 days. The above risks associated with midlines would therefore be lower given the brief dwell time.

Considering the invasive nature of CVCs and their associated logistical issues, midline catheters represent an appealing alternative. They may not, however, be an option in all patients. Donors with small arm veins or pre-existing PICC lines are unlikely candidates. Prior to initiation of mobilization, and preferably following any chemo-mobilization, prospective donors should undergo vein assessment to evaluate for presence of PICC lines or adequate surface veins. In patients without adequate surface veins, ultrasonography of the arm veins should be conducted to assess suitability of upper arm veins prior to pursuing collection via a midline catheter option. CVCs may still be required in some donors. Finally, close coordination between all teams, including the vascular access team, is needed to avoid delays in start of collection.

CONFLICT OF INTEREST STATEMENT

The authors have disclosed no conflicts of interest.

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