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Randomized pilot study to compare metal needles versus plastic cannulae in the development of complications in hemodialysis access

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Abstract

Background: Hemodialysis requires needle insertions every treatment. Needle injury (mechanical or hemodynamic) may cause complications (aneurysms/stenosis) that compromise dialysis delivery requiring interventions. Metal needles have a sharp slanted "V"-shaped cutting tip; plastic cannulae have a dull round tip and four side holes. Preliminary observations demonstrated a difference in intradialytic blood flow images and mean Doppler velocities at cannulation sites between the two devices. Complications from mechanical and hemodynamic trauma requiring interventions were compared in each group.

Materials and methods: In all, 33 patients (13 females and 17 new accesses) were randomized to metal group (n = 17) and plastic group (n = 16). Mechanical trauma was minimized by having five nurses performing ultrasound-guided cannulations. Complications were identified by the clinician and addressed by the interventionalists, both blinded to study participation. Patients were followed for up to 12 months.

Results: Baseline characteristics were not significant. Procedures to treat complications along cannulation segments increased from 0.41 to 1.29 per patient (metal group) and decreased from 1.25 to 0.69 per patient (plastic group; p = 0.004). The relative risks of having an intervention (relative risk = 1.5, 95% confidence interval = 0.88–2.67) and having an infiltration during hemodialysis (relative risk = 2.26, 95% confidence interval = 1.03–4.97) were higher for metal needles. Time to first intervention trended in favor of plastic cannula (p = 0.069). Cost of supplies for these interventions was approximately CAD$20,000 lower for the plastic group.

Conclusion: Decreased burden of illness related to cannulation (less infiltrations during hemodialysis) and Qb were associated with plastic cannulae. Decreased procedure costs were suggested during the study period in the plastic group.

Keywords

Metal needle, plastic cannulae, aneurysm, stenosis, ultrasound

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Introduction

The requisite insertion of two needles for every hemodialysis (HD) treatment is attended by needle injury due to both mechanical and hemodynamic trauma (related to the pump speed (Qb) during HD). Needle injury with cannulation may cause deleterious effects to the patient's vascular access that ultimately requires radiological or surgical procedures to maintain or to restore patency.[1] These interventions add significant therapeutic burden to this patient population, as well as cost burden to the health-care system.[2]

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The major scientific inquiries on the complications of vascular access for HD focus on the development of neointimal hyperplasia (NIH) of juxta-anastomotic sites in arterio-venous fistulae (AVF), mostly responsible for primary failure, and on complications at the venous anastomosis of arterio-venous grafts (AVG). Furthermore, this scientific focus attempts to identify therapies to prevent or treat these complications to establish or prolong the use of the HD access.[1,3–9] The mechanical trauma and altered hemodynamics due to cannulation and Qb during HD likely generate the development of access stenosis or aneurysms distinct from the lesions in the peri-anastomotic areas.[10–16] The contribution of the repeated mechanical trauma and healing due to the placing of the devices and then the additional hemodynamic trauma resulting from Qb during HD per se need scientific attention.

There are two cannulation devices with different designs and configurations. Metal needles use a sharp slanted "V" cutting edge to enter the vessel and they have a back eye. Plastic cannulae are introduced with a metal needle guide with a 17G cutting edge that is removed once the plastic cannula is in the vessel. Plastic cannulae have a symmetric round tip and four side holes within 0.5 cm from the tip and a 15G shaft (Figure 1). Plastic cannulae are used during the first 2–4 weeks of cannulation of new or complex accesses for their lower risk of infiltration compared to metal needles;[11,13,14,17,18] their use can be extended in patients with high risk of infiltration. The primary reason to transition cannulae to metal needles is cost; they are 2–3 times more expensive than metal needles. Preliminary studies demonstrated that blood flow image patterns during dialysis differed between metal needles and plastic cannulae and that mean Doppler velocities of the blood flow were significantly higher for metal needles than for plastic cannulae.[11] These clinical findings are consistent with early pre-clinical studies[19–23] and with more recent computational hemodynamic mathematical models showing a high-speed jet stream forming from a metal needle directed to the vessel wall.[24–26] The impact of blood flow disturbances, attributable to the augmented flow generated by the pump speed (Qb) per se, in the development of complications that require interventions along cannulation sites comparing metal needles and plastic cannulae is not known. The objective of this study was to assess the feasibility of conducting an informative randomized controlled trial (RCT) comparing the two cannulation devices in the development of complications requiring diagnostic or surgical interventions.

Methods

Study design

Prospective randomized controlled pilot study to compare metal needles versus plastic cannulae in the development of complications (aneurysms and stenotic lesions) along cannulation sites in arterio-venous access of HD patients. The study was approved by the Research Ethics Board of the institution and all study subjects provided informed written consent.

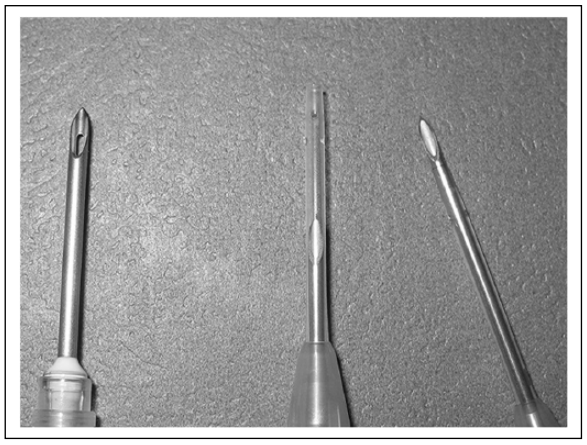

Figure 1. Metal needle (left) and plastic cannula (center: metal guide retracting, right: plastic cannula in situ).

Study population

All patients attending the in-center chronic HD program at a large community hospital were considered for participation. The study population of 33 subjects derived from a cohort of 420 patients as detailed in Figure 2. Subjects were eligible for participation if they had a functioning AV access and were able to provide written informed consent. Potential subjects were excluded if they were required to use plastic cannula beyond the usual 30-day clinical standard (the standard of care in this unit is that patients are not transitioned to metal needles in cases of marked restlessness or severe bruising). They were also excluded if they had cognitive or language barriers or if they had an acute medical illness that impaired their ability to provide informed consent.

Study co-interventions

Vascular access evaluation. The standard of clinical practice in this HD program was that a single surgeon evaluated all accesses in the vascular access clinic before and after the access creation or a radiologic/surgical intervention. Routine Doppler ultrasound studies (DUS) were performed at 1 week post creation and prior to initiation of cannulation as well as after radiological interventions. Incident accesses were deemed appropriate for cannulation when the Disease Outcomes Quality Initiative (DOQI) rule of 6's criteria for cannulation were met.[27] All accesses had at least one 7-cm-long cannulation segment.

Cannulation protocol and use of ultrasound. To standardize cannulation and minimize needle trauma caused by variation

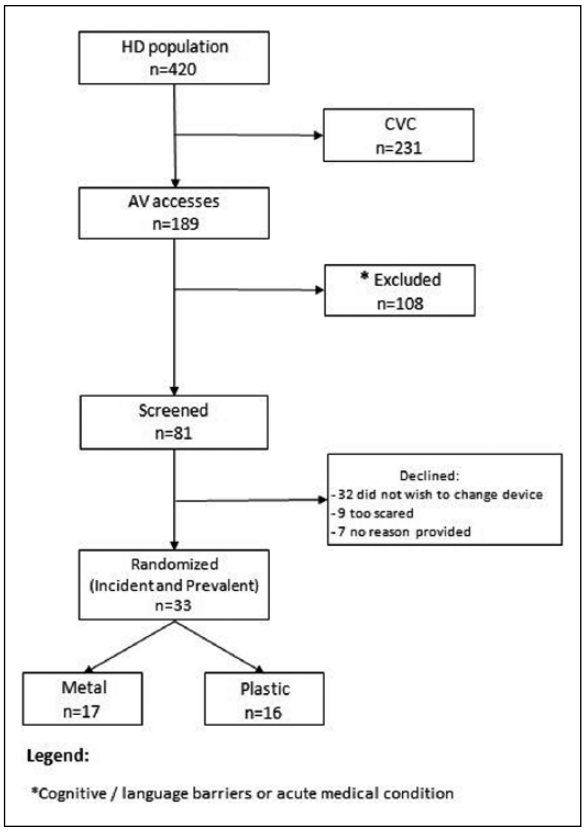

Figure 2. Subject flow diagram.

in skills and practice, cannulations were conducted in a controlled environment with the use of real-time ultrasound guidance by a group of five nurses with advanced level of competency in the use of point-of-care ultrasound.[28–30]

Rope-ladder technique was used in all patients, and the needle lengths were chosen according to the depth of the cannulation segments.[13] Needle insertions were rotated systematically to avoid aneurysms, vein in junctions, vein valves, or veins overlying the puncture areas. Needles were at least 2 in apart,[27,31] and to maximize needle rotation, longer needles were used if cannulation segments were >0.6 cm of depth. Retrograde orientation for the arterial needle was used to maintain adequate distance between the two needles when required. Needle insertions were performed in one single stroke. During cannulation, needle tips were positioned at the center of the vessel lumen, and after securing the devices with tape, their position was verified by manual confirmation of no resistance (standard practice) as well as visual confirmation of the 10 mL bolus of normal saline. During dialysis, ultrasound was used for needle repositioning triggered by pressure alarms. Study patients were evaluated within 2 h of initiation of treatment to ensure that the prescribed Qb had been achieved. Cannulations were videotaped and documented in the vascular access team documentation record. Cannulation complication videos were reviewed by two members of the cannulation team for the assessment of severity.

Management of clinical complications

Blood extravasations during cannulation were controlled under ultrasound with a 10-min gentle four-finger pressure without needle removal, after which ice therapy was applied. If unable to proceed due to pain or vascular spasms, cannulation was postponed.

Blood infiltrations during dialysis treatment were evaluated by two members of the cannulation team. If unable to correct the problem with needle repositioning or recannulation, the dialysis treatment was postponed. All patients with clinical complications were instructed to apply ice therapy at home for 20 min 3 times a day. Areas of bruising or with hematomas were avoided for cannulation, and their progression to resolution was monitored with ultrasound at each subsequent treatment.

Equipment and cannulation devices. The cannulation devices were 15G caliber (1.8 mm) metal needles (Nipro Safe-Touch II; Nipro Medical Corporation) and 17G caliber (1.9 mm) plastic cannulae (Safety Clampcath sp 302; Togo Medikit Co, Ltd.) both available in 1″ (25 mm) and 1¼″ (33 mm) in length.

The ultrasound devices were Sonix Touch (Ultrasonix Medical Corporation) and SonoSite S-Cath™ US system (SonoSite Canada).

Cost calculation. The cost of the supplies utilized during the procedures as indicated in the dictated medical reports was estimated. There was variation in the type of supplies used by each of the interventionalists and surgeon. To minimize preference bias with the selection of specific supplies and equipment during a procedure, only the cost of the basic disposable setup tray was used as the unit cost for the procedure. The cost was similar for both the interventional and the surgical basic setup trays and was estimated to be CAD$2500. The cost of metal and plastic cannulae was obtained from the unit cost of the devices multiplied by the number of dialysis treatments in the two groups. The unit cost of the metal needle was CAD$1 and that of the plastic cannulae was CAD$3. The cost/patient-month was estimated by dividing the total cost of the procedures and devices by the mean total treatments per patient-month. Cost of personnel was not factored in the calculation.

Access outcome evaluations. Transonic access flows (QA), Qb (the average reported from the entire session), as well as parameters of dialysis adequacy (Kt/V and PRU) were obtained every 6 weeks as per the standard practice in the HD unit.

Study outcomes

The primary outcome of this study was the proportion of patients who had a procedure for stenosis, thrombosis, or aneurysmal formation along the cannulation segments by

the end of 1 year. Secondary outcomes included the number of procedures per patient, time to first event, adequacy of dialysis, cannulation complications (during cannulation and during HD), logistical consequences of cannulation complications (missed dialysis treatments and shorter dialysis), and cost.

An aneurysmal dilatation was defined as an enlargement of >50% of the diameter compared to the adjacent vessel. Aneurysmal repairs were triggered by an enlargement of 2–3 times the diameter of the access compared to baseline, accompanied by skin changes/presence of erosion, a clot formation with flow obstruction, or the need to repair the affected wall to rescue a cannulation segment.

Aneurysmal and stenotic areas were evaluated with DUS, and the adjudication of severity and referral for treatment were done by the rounding nephrologist or vascular surgeon. Complications requiring radiological interventions were triggered by a decrease of QA >30% compared to baseline, or the development of stenosis of >50% decrease in diameter compared to the adjacent vessel, and/or the inability to achieve the prescribed Qb in spite of confirmation of an adequate intraluminal needle position. Blinding in this intervention trial is optimal to minimize bias in treatment and in triggering the outcomes of interest. As per institutional policy, the devices were not covered during dialysis treatments due to the safety concerns of a delay of recognizing accidental needle dislodgement. Therefore, patients were not blinded to the device, but the triggers and clinical interventions would be largely independent of factors that could be modified by patients. While the nurses providing the HD treatment would be aware of the device, they may or may not be aware of the patient's participation in the study. Furthermore, the complications that would trigger an intervention would be assessed by the primary nephrologist, who also would not be aware of their participation. Finally, the interventionalists or surgeon treating the complications were blinded to participation of the patients in the study. Acknowledging the merits of blinding, the logistical challenges are highlighted.

Randomization scheme

Patients were randomized in a 1:1 ratio to metal needles or plastic cannulae using a randomization computer-simulated protocol (online GraphPad software) and using closed envelopes prepared by a research assistant not involved in the study.

The standard clinical practice in this unit is the use of plastic cannulae for the initial 4 weeks of use of the access, and then, cannulation is transitioned to the use of metal needles. Therefore, the incident patients were randomized after 4 weeks of cannulation with plastic cannula to either transition to cannulation with metal needles or to continue cannulation with plastic cannulae. Prevalent patients, however, were using metal needles, and hence, their randomization was to remain on the standard care with metal needles or switch to plastic cannula for the duration of the study.

Statistical analysis

The primary outcome of this study was the proportion of patients in each group who required an intervention during the 1-year follow-up. The primary analysis was an intention-to-treat approach with an a priori plan to perform a sensitivity analysis for cross-over or withdrawals.

Descriptive statistics were used to present baseline demographic and clinical characteristics including age, gender, dialysis vintage, and access vintage (incident or prevalent) in the two study groups. Normally distributed data are presented with means and standard deviations, and Student's t-test was used to compare differences between the two groups. Categorical data are presented as frequencies (percentages) and compared using chi-squared differences in proportions with 95% confidence interval (CI) for binary outcomes. Small sample size comparisons between groups were made with chi-squared and Fisher's exact test. Relative risks (RRs) of having an event comparing the two groups were also calculated. Data that did not have a normal distribution were compared using the Wilcoxon signed-rank test. Kaplan–Meier curves were used to display time to first event. Log-rank test was used to compare differences in event-free survival between the two groups. A subgroup analysis of incident and prevalent patients was also conducted. An a priori logistic regression model was planned to assess for the presence of an interaction of the type of needle device and the vintage of the access (incident and prevalent). Statistical software IBM SPSS statistics for Windows (Version 22.0; IBM Corp.) was used for all statistical analyses in this study.

Results

A total of 33 subjects participated in the study from April 2013 to August 2015. Table 1 shows the baseline demographic characteristics of the study participants. Patients were randomized to metal (n = 17) or plastic (n = 16) and were followed for up to 13 months from study entry: mean follow-up of 8.9 months/patient in the metal group and 10.9 months/patient in the plastic group. There were no significant differences in sex, age, HD vintage, cause of renal disease, or type of location and vintage of the vascular access.

There were 17 incident accesses, 9 (53%) in the metal group and 8 (50%) in the plastic group), and 16 prevalent accesses (50% in each group). There were 30 AVFs, 2 mixed accesses with a short interposition graft (only the native vein portion was used for cannulation) and 1 HeRo graft with standard expanded polytetrafluoroethylene (ePTFE) material. One patient randomized to the metal

Table 1. Baseline characteristics of the study population.

Patients	Metal	Plastic	*p*
Characteristics			
N	17	16	
Sex: male	9 (53%)	11 (69%)	0.353
Age (years)	62 (15)	62 (14)	0.978
HD vintage (years)	2.2	2.7	0.321
Access vintage (days)	390 (537)	531 (512)	0.446
Mean follow-up period (months)	8.9	10.9	
Etiology (ESRD)			
Diabetes mellitus	9 (53%)	11 (69%)	0.353
Glomerulonephritis	4 (24%	0	0.103
Vascular disease	3 (18%)	3 (19%)	0.941
Other/unknown	1 (6%)	2 (13%)	0.601
Type of access			
AVF	17 (100%)	13 (81%)	0.063
Graft interposition	0	2 (13 %)	0.130
HeRo graft	0	1 (6%)	0.684
Upper arm	12 (71%)	10 (63%)	0.622
Incident access	9 (53%)	8 (50%)	0.865
Prevalent access	8 (47%)	8 (50%)	0.866

HD: hemodialysis; ESRD: end-stage renal disease; AVF: arterio-venous fistulae; SD: standard deviation.
Percentage and SD values are given in parentheses.

group had an infiltration with a large hematoma during the first month of the study and required to continue cannulations with plastic cannulae.

Clinical evaluations of blood pressure, pulse, QA, Qb, PRU, and Kt/V did not show any significant difference between the two study groups at 1, 3, 6, 9, or 12 months (Table 2). Subgroup analysis of the incident and prevalent groups separately did not show statistical significance (results not shown).

The outcome data summarize the procedure events for the total group and the subgroup analyses for incident and prevalent accesses as well as the clinical complications which are presented separately in Table 3. All procedures to assist maturation or to repair or maintain access function that occurred from the time the access was created to the initiation of the study were considered baseline events. There were a total of 21 patients who had at least one event. Out of 17 patients, 13 (76.5%) and out of 16 patients 8 (50%) had at least one event in the metal and plastic groups, respectively ($p=0.14$). The mean number of events per patient was 0.41 and 1.25 in the metal and plastic groups, respectively, at baseline ($p=0.019$) and 1.29 and 0.69 in the metal and plastic groups, respectively, during the study period ($p=0.081$). Within the metal and plastic groups, the mean difference was 0.88 and −0.56, respectively ($p=0.004$). The subgroup analysis of incident and prevalent groups presented in Table 3 identified the difference as being derived from the prevalent group ($p<0.001$).

Table 2. Mean clinical characteristic evaluations.

Patients	1 month			3 months			6 months			9 months			12 months		
	Metal	Plastic	*P*	Metal	Plastic	*P*	Metal	Plastic	*P*	Metal	Plastic	*P*	Metal	Plastic	*P*
N	17	16		17	16		17	16		17	16		17	16	
SBP	135 (22)	141 (22)	0.487	148 (19)	150 (26)	0.790	141[a] (26)	155[b] (27)	0.164	152[c] (26)	150[d] (23)	0.899	143[c] (30)	160[e] (14)	0.202
DBP	71 (12)	67 (13)	0.427	80 (12)	73 (17)	0.198	73[a] (13)	72[b] (25)	0.940	79[c] (19)	75[d] (20)	0.663	68[c] (21)	72[e] (14)	0.700
PULSE	77 (11)	78 (13)	0.802	76 (13)	77[a] (12)	0.785	76[a] (12)	75[b] (14)	0.949	81[c] (18)	76[d] (14)	0.578	83[c] (21)	74[e] (11)	0.329
QA	1127 (609)	932[b] (490)	0.343	1157 (769)	1041[a] (620)	0.645	1051[a] (603)	1029[b] (511)	0.917	1210[e] (560)	1141[e] (593)	0.804	1427[e] (973)	1084[e] (507)	0.363
Qb	282 (48)	291 (34)	0.516	294 (44)	305 (42)	0.507	289[a] (40)	302[b] (29)	0.342	304[c] (18)	335[d] (63)	0.229	305[c] (45)	305[e] (19)	0.977
PRU	0.75[f] (0.06)	0.76 (0.06)	0.713	0.77[f] (0.07)	0.78[f] (0.18)	0.741	0.75[a] (0.06)	0.75[b] (0.08)	0.939	0.77[e] (0.05)	0.74[g] (0.07)	0.251	0.77[e] (0.05)	0.76[d] (0.05)	0.714
KT/V	1.64[b] (0.28)	1.63[b] (0.26)	0.910	1.57[b] (0.31)	1.55[a] (0.39)	0.845	1.59[h] (0.31)	1.57[b] (0.29)	0.868	1.62[c] (0.28)	1.64[d] (0.24)	0.847	1.55[i] (0.28)	1.70[d] (0.24)	0.285

SBP: systolic blood pressure; DBP: diastolic blood pressure.
[a]n = 14, [b]n = 16, [c]n = 15, [d]n = 13, [e]n = 9, [f]n = 7, [g]n = 10, [h]n = 11, [i]n = 5.

Table 3. Event summary by study group and clinical complications.

Primary analysis			
Total group	Metal (n = 17)	Plastic (n = 16)	*p*
No. patient requiring interventions	13 (76%)	8 (50%)	0.140
Baseline number of events per patient[a]	0.41 (0.7)	1.25 (1.2)	0.019
Mean number of events per patient	1.29 (1.1)	0.69 (0.8)	0.081
Mean difference	0.88 (1.3)	−0.56 (1.4)	0.004
Days to first event	158 (105.5)	132 (98.5)	0.582
Mean survival days	162 (109.6)	231 (138.3)	0.120
	Subgroup analysis		
Incident group	Metal (n = 9)	Plastic (n = 8)	*p*
Baseline number of events per patient[a]	0.44 (0.9)	0.38 (0.5)	0.848
Mean number of events per patient	1.11 (1.3)	0.63 (0.7)	0.359
Mean difference	0.67 (1.7)	0.25 (1.2)	0.575
Days to first event	190 (112.8)	166 (134.2)	0.762
Mean survival days	183 (123.7)	232 (142.5)	0.455
Prevalent group	Metal (n = 8)	Plastic (n = 8)	*p*
Baseline number of events per patient[a]	0.38 (0.5)	2.13 (1.0)	0.001
Mean number of events per patient	1.5 (0.9)	0.75 (0.9)	0.120
Mean difference	1.13 (0.6)	−1.38 (1.1)	<0.001
Days to first event	131 (98.8)	99 (40.9)	0.560
Mean survival days	138 (93.4)	229 (143.6)	0.156
Number of clinical complications[b]	Metal (n = 17)	Plastic (n = 16)	*p*
Total complications	18 (1.06 ± 0.66)	7 (0.44 ± 0.51)	0.005
Blood extravasation during cannulation	4 (0.24 ± 0.56)	2 (0.13 ± 0.34)	0.50
Infiltration during HD with HD short/loss	14 (0.82 ± 0.64)	5 (0.31 ± 0.48)	0.014
Infiltration during HD with treatment loss	2 (0.12 ± 0.33)	0 (0)	0.16
Number of patients with clinical complications	Metal (n = 17)	Plastic (n = 16)	*p*
Total number of patients with clinical complications	14 (83%)	7 (44%)	0.021
Infiltrations during cannulation	3 (18%)	2 (13%)	1.000
Infiltrations during HD	12 (71%)[c]	5 (31%)[d]	0.038

[a]Number of events from creation: percentage and SD values are in parentheses.
[b]Number of complications: mean and SD values are in parentheses.
[c]Metal needles pierced through the vessel wall.
[d]Cannulae were retracted from the vessel.

There were a total of 25 clinical complications related to mechanical trauma (in 21 patients): 18 (1.06 ± 0.66) in the metal group (in 14 patients) and 7 (0.44 ± 0.51) in the plastic group (in 7 patients; p = 0.005). Blood extravasations during cannulation were similar in both groups (p = ns):4 (metal) and 2 (plastic). Infiltrations during HD were 14 (0.82 ± 0.64) in metal and 5 (0.31 ± 0.48) in plastic (p = 0.014). Two of the infiltrations in the metal group required treatment discontinuation in order to rest the access. No patient required the insertion of a central venous catheter during the study. A total of 21 patients had clinical complications: 14 (83%) in the metal group and 7 (44%) in the plastic group (p = 0.021). Three patients had blood extravasations in the metal group compared to two patients in the plastic group (13%, p = ns). Infiltrations during HD occurred in 12 patients in the metal group (71%) and in 5 patients (31%) in the plastic group (p = 0.038). The RR of an infiltration was approximately double for metal needle compared to plastic cannulae (RR = 2.26, 95% CI = 1.03–4.97).

The types of interventional procedures to treat complications and associated cost estimates by study group are presented in Table 4. At baseline, there were a total of 27 procedures, 7 (26%) for the metal and 20 (74%) for the plastic group compared to 33 procedures during the study 22 (67%) for the metal and 11 (33%) for the plastic group. In all, 13 patients had at least one procedure in the metal group and 8 patients had at least one procedure in the

Table 4. Procedures and cost estimates by study group.

Procedures	Metal (n = 17)		Plastic (n = 16)	
	Pre[a]	Post	Pre[a]	Post
Surgical				
Stenosis repair	2	3	3	1
Aneurysmal repair—cannulation sites	1	0	2	1
Radiological				
Juxta-anastomosis angioplasty	4	0	1	0
Angioplasty at cannulation sites	0	18	10	9
Angioplasty with thrombolysis	0	1	4	0
Total	7 (26%)	22 (67%)	20 (74%)	11 (33%)
Costs estimates	Metal (n = 17)		Plastic (n = 16)	
Total HD treatments	1966		2269	
Mean duration of follow-up (months)	8.9		10.9	
Cost of cannulation device	CAD$3932		CAD$13,776	
Estimated cost of procedures	CAD$55,000		CAD$27,500	
Total cost per study period	CAD$58,932		CAD$41,276	
Estimated cost/patient-month	CAD$6622		CAD$3787	

[a]Number of interventions from creation. All values are in Canadian dollars.

plastic group (p = 0.14). The RR of requiring a procedure when using a metal needle was 1.52 (95% CI = 0.90–2.67, p = ns). Kaplan–Meier displays of time to first event are shown in Figure 3 for the total group and for the subgroup analyses of the incident and prevalent groups. For the total group, the difference in event-free survival trended in favor of plastic cannulae (p = 0.069). A sensitivity analysis was also conducted with and without the patient who crossed-over from the metal into the plastic cannula. There were no statistical differences in the results (data not shown).

Costs of the cannulation devices and the basic procedural tray for the interventions by study group are shown in Table 4. The metal group had a total of 22 procedures, while the plastic group had 11 procedures representing costs of CAD$55,000 and CAD$27,500, respectively. The costs of the devices per se were CAD$3932 for metal needles to provide 1996 HD treatments and CAD$13,776 for the plastic cannulae to support 2296 HD treatments. The total estimated cost/patient-month was CAD$6622 for the metal group and CAD$3787 for the plastic cannula.

Discussion

This study was informative in that it demonstrated the feasibility of conducting a cannulation study to compare metal needle versus plastic cannulae in the development of complications at cannulation sites in HD access conducted in a controlled environment.

In spite of randomization, there were statistical differences in the baseline number of events/patient in the two groups. It was significantly lower in the metal group compared to the plastic group (0.41 vs 1.25, p = 0.019). At the end of study, the number of procedures increased in the metal group and decreased in the plastic group (1.29 vs 0.69, p = 0.081), and the mean difference between the groups was significant (0.88 vs −0.56, p = 0.004). With marked differences at baseline, the possibility of an overestimation of the effect size of the intervention exists. The decrease in procedures in the plastic group could have been confounded with regression to the mean. However, in this study, the association of the biological aspect of *ongoing* injury with cannulation and the development of complications were also considered.

The trauma associated with HD needle insertions is complex. The mechanical trauma related directly to the needle placement includes the biological injury to the wall of the vessel. In addition, blood extravasation due to accidental piercing through the vessel wall or trauma at the time of needle removal may generate hematomas that distort the geometry of the access which, when severe, may cause flow obstruction with increased risk of thrombosis and access loss.[11] Mechanical trauma is amplified with poor needle rotation (area puncture) that is seen in accesses with short cannulation segments (<7 cm)[2,32–37] or in situations of poor clinical practice where rope-ladder rotation is inadequately performed causing destruction of the elastic lamina and aneurysmal distension of the anterior wall in an AVF and destruction of the graft material with pseudo aneurysm formation in an AVG.[38–41]

In this study, there were a total of 25 clinical complications of blood extravasation (during cannulation) or infiltration (during HD) related to mechanical trauma. A total

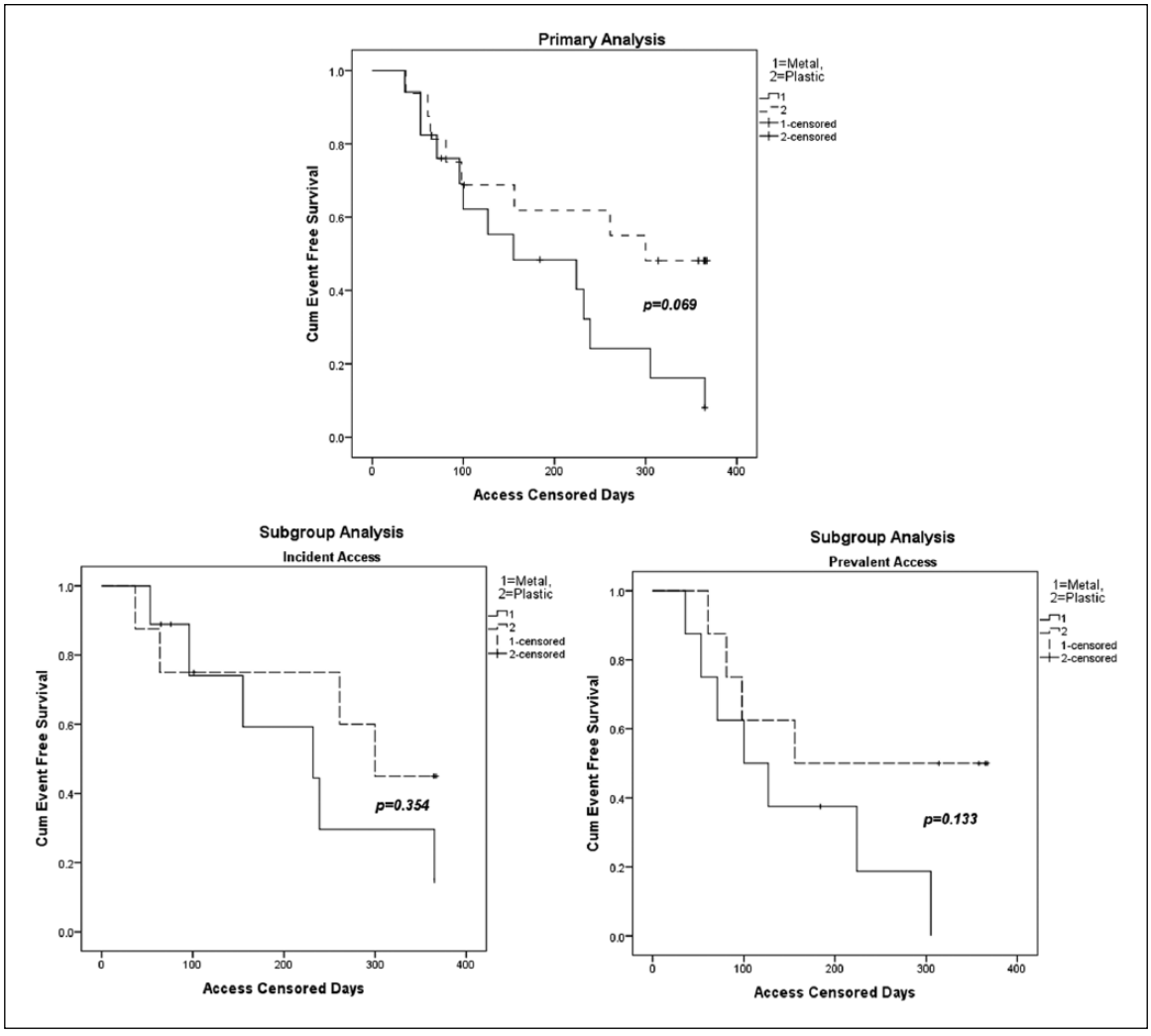

Figure 3. Time to first event: study group (top) and subgroups (bottom).

of six blood extravasations occurred from the needle puncture entry site after a successful needle placement without downstream flow obstruction. A possible explanation for these complications is the variability of wall thickness across the cannulation segments and hence the potential hoop strength that is required to withstand repetitive cannulation. An intimal-media wall thickness (IMT) of ≥0.13 mm measured with high-frequency ultrasound has been found to be associated with successful cannulations.[12] IMT measurements were not obtained in this study. Blood extravasations during cannulation were controlled without sequelae.

The frequency of trauma associated with infiltration during dialysis was 2.3 times higher for metal needles compared to plastic cannulae. Infiltrations were usually related to sudden involuntary movements of the patient. In such cases, metal needles were observed to have pierced through the vessel wall, while plastic cannulae were found to have retracted from the intraluminal space.

Beyond puncture trauma, the hemodynamic effect of blood flow disturbances at needle sites during dialysis (Qb) or generated by distortion of the geometry of the vessels by hematomas or at aneurysmal sites may alter shear stress and activate endothelial response to injury, responsible for NIH, smooth muscle cell migration, and formation of stenotic lesions.[35,42–46]

This study was conducted in a controlled environment in order to minimize the noise caused by variation in clinical cannulation skills. Cannulations and needle repositioning, when required, were performed with the use of real-time ultrasound guidance to "*Picture Perfect Cannulation*" and to prevent accidental puncture through the back wall or damage to the endothelia by blind needle repositioning (without ultrasound assistance). In this context, the mechanical trauma caused during needle insertions was minimized to enhance the signal of the hemodynamic effect of blood flow disturbances caused by the two types of cannulation devices during dialysis produced by Qb. Blood flow

patterns differ with the two types of devices. The plastic cannulae generate a blood flow toward the center of the vessel; in contrast, metal needles generate a jet stream directed to the vessel wall.[11]

The baseline procedures consisted of angioplasties to assist maturation in the incident fistulae and to treat stenotic areas or surgical repairs of aneurysmal sites and angioplasties of the cannulation sites in prevalent accesses.

The damaging effect of diagnostic interventions and surgical manipulation is well known. Stenotic lesions can reoccur after angioplasty procedures and sometimes with an accelerated time course.[1,9,47–49] Taking into consideration the biological effect of the higher number of procedures at baseline and their inherent vascular damage in the plastic group, one could have anticipated a further increase in the need for procedures, but, on the contrary, the opposite was observed. In contrast, while the metal group had a lower baseline rate of procedures, they required a higher number of procedures compared to baseline over the course of the study.

While the findings suggest that the use of metal needles may be associated with a clinically important increased risk of having a complication that requires intervention compared to plastic cannulae (RR = 1.5, 95% CI = 0.9–2.6, p = ns), this pilot study had a small sample size and was not powered to detect a statistical difference (power = 32%). These results were consistent in the subgroup analysis of the prevalent accesses.

With respect to dialysis adequacy, there was no significant difference in performance with the two devices as measured by PRU and Kt/V which contrasts with some uncontrolled studies that suggest that dialysis performance with plastic cannulae may be lower than with metal needles. The prescribed Qb (300–400 mL/min) were achieved with the two devices without triggering pressure alarms. The equivalent pressure profiles may be explained by the plastic cannula's design with four additional side holes, which allows for even distribution of the pressure along the cannulae.

The use of needle lengths that accommodated uneven depths with areas of >0.6 cm of depth along cannulation segments allowed adequate rotation of cannulation sites. No aneurysmal sites developed in any of the incident accesses (Figure 4). Aneurysmal areas were present at baseline in the arterial or the venous cannulation segments in the prevalent accesses, and these were avoided for cannulation. No new aneurysmal sites developed in the prevalent accesses. It was observed that the size of the aneurysms decreased in two patients in the plastic cannula group without any added intervention (i.e. an angioplasty of a flow obstructing stenotic area), change in access flows, or blood pressure. In the metal group, one patient had an aneurysmal site that maintained its diameter and did not require a surgical repair by the end of the study. This could be a result of, first, avoiding systematically overused areas for cannulation, second, avoiding blood flow disturbances in the aneurysmal site by having the venous needle positioned upstream and beyond the enlargement, and, third, having the plastic cannula puncture with a smaller cutting edge of a 17G tip compared to a 15G tip from metal needles. One prevalent patient in the plastic cannulae group had a preexisting aneurysm that was repaired to rescue a cannulation segment. The direct cost of the basic disposable supplies required for the procedures to address the complications was estimated from the clinical notes wherein the radiological/surgical procedures were documented. The costs of the devices detailed therein were verified with the purchasing department. The estimated cost of CAD$2500 is consistent with the cost calculated by Manns et al.[50] Notwithstanding that the actual costs of the devices per se were higher for the plastic cannulae, the patient-level costs for treatment overall were less for the cannulae by approximately CAD$20,000 for 16 patients. So, scaling a minimal cost savings of approximately CAD$2000 per patient per year would be fiscally important in addition to the lower procedural burden experienced by the patients.

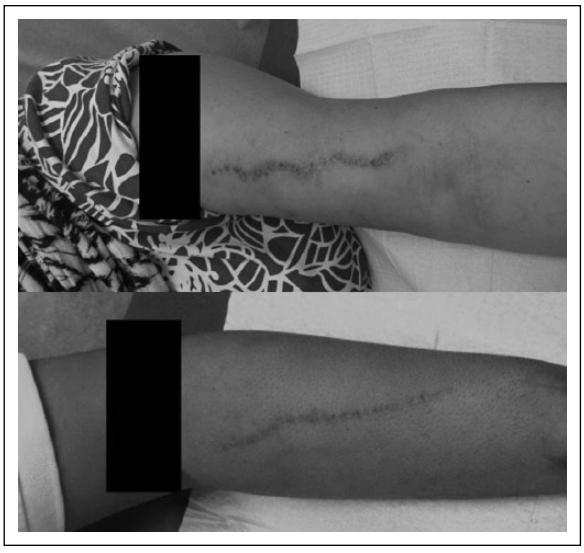

Figure 4. Rope-ladder technique in incident patients: note needle rotations marks along cannulation segments in upper arm (top) and lower arm accesses (bottom) without aneurysmal formation.

This study has a number of limitations, foremost being the lack of blinding. Blinding the cannulation devices was deemed to introduce an indefensible element of risk in the event of an accidental dislodgement during dialysis. To minimize the potential effect of systematic bias, the clinical parameters that would trigger the need for consideration of an intervention followed well-defined pre-specified quantitative functional parameters of the standard of clinical practice. The physician identifying the complications as well as the interventionalist or surgeon treating them did so in course of their usual clinical participation of the care of these patients. Like the other health-care professionals involved in the care of these patients, they may have

remained unaware of the patient's participation in the study, but this was not validated.

Second, while the expertise of the cannulators was of value in minimizing and controlling the mechanical trauma, this element is relevant in consideration of the generalizability of the results to most clinical programs. Complications related to needle insertions are common, and most patients have at least one within the first few months of use of the access. Van Loon et al.[34] reported a cannulation success of 9% for all HD treatments (~6 months follow-up) without ultrasound assistance. In our study, the use of ultrasound for all cannulations optimized needle insertions, and 85% of the patients underwent successful cannulations for all HD treatments during the study period. The practical aspects of using ultrasound for all cannulations in standard clinical practice require further scientific evaluation. One must also consider that cannulation with plastic cannulae requires a different cannulation skill set that requires training and practice to be successful.[18] While this was a critical aspect in the conduction of this study, this concern was mitigated by the fact that in this HD program, the standard of practice for cannulation of all new and complicated accesses is to use plastic cannulae, and therefore, the nurses already had this skill set. Furthermore, the use of ultrasound guidance enhanced the basic skill set of cannulating with plastic cannulae.

From a technical perspective, the use of different needle lengths and calibers may have had an impact in hemodynamics at needle sites. The use of longer needles was clinically adequate and allowed for proper rotation of cannulation sites in areas >0.6 cm of depth from the skin surface. With a systematic needle rotation, the jet stream was also rotated in the cannulation segment minimizing the exposure to hemodynamic injury to the same area.

The pilot study demonstrated some logistical challenges of conducting a cannulation study in a clinical setting. The controlled environment, achieved by highly skilled cannulators and the use of real-time ultrasound guidance, generated the logistics of ensuring the availability of one of the five cannulators that would be formidable in the usual clinical setting. As well, the blinding issue as referred to above remains a formidable, if not insurmountable, element in the design of a double-blinded trial of cannulation devices.

Access damage or access loss due to poor cannulation is a serious practice problem; it increases patient's morbidity and cost to the health-care system and has potential legal consequences. This study intensified the appreciation for the importance of optimal cannulation in prolonging access survival and of the need of an appropriately powered randomized clinical trial.

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