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## Blood Access Outcomes Associated with Short Daily Hemodialysis

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**W**ith the growing number of reports that daily hemodialysis (DHD) improves clinical outcomes and quality of life, there has been increased interest in the effects of more frequent venipunctures on blood accesses. Since 1996, we have converted 30 patients (27 in-center, 3 home) from conventional 3/week dialysis to short, daily, 6/week dialysis (sDHD). Twenty-five patients started for medical indications. End-stage renal disease (ESRD) causes were diabetes mellitus (in 7), hypertension (6), glomerulonephritis (8), hereditary nephritis (2), and other (7). Mean ( $\pm$ SD) age was  $57 \pm 16$  years. Patients had an average of 3.8 major comorbidities in addition to ESRD. Thirty patients were followed on sDHD for 388 patient-months: 9 patients died after  $4.2 \pm 6.7$  months, 3 were transplanted at  $5.4 \pm 2.2$  months, and 3 were disenrolled at  $9.3 \pm 10.5$  months. Fifteen patients remain on sDHD at  $20.4 \pm 14.1$  months. Access problems for the 12 months prior to sDHD were compared to those that occurred while the patient was on sDHD. Problems were tracked by access type. There were 40 different accesses in 30 patients with a cumulative 28.07 access-years pre-DHD; 24 of these accesses were artificial bridge grafts (ABG) of either polytetrafluoroethylene or bovine material. There were 27 access problems pre-DHD, or 0.962 problems per access-year. On sDHD these same 30 patients had 41 accesses for 34.44 access-years; 23 of these were ABGs. There were 31 access problems or 0.900 problems per access-year. There were no significant differences in access problems comparing pre-DHD with on-sDHD, either in aggregate or when analyzed by access type. After 39 months of observation, there does not appear to be an increase in blood access problems when patients are converted from conventional dialysis to sDHD.

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### Key words

Daily hemodialysis, blood access, catheters, fistulas, grafts

### Introduction

A growing number of reports describing outcomes for patients converted to daily hemodialysis (HD) are striking in the similarity of their findings. Consistently, patients on short six-times-weekly dialysis (sDHD) are reported to have improved

clinical outcomes and quality of life [1–6]. A persistent and unanswered concern, however, is how blood accesses would fare with increased use. If vascular access is the Achilles' heel of HD now, it is feared it may be twice the existing problem for those on daily HD. Often the first medical concern expressed by patients or nephrologists when considering this modality is whether fistulas/grafts will develop increased complications or failures from more frequent use.

While there are some early reports on the outcomes of natural arteriovenous fistulas (AVF) [2,5] and tunneled central-vein “permanent” catheters (PC) [7] with sDHD, there are no comparative reports of outcomes of arteriovenous bridge grafts (ABG).

In October 1996, El Camino Dialysis Services started a sDHD program. El Camino Hospital, a nonprofit community hospital in Mountain View, California, was willing to underwrite the additional unreimbursed treatments in order to make this therapy available to those patients failing on conventional HD. Short DHD was, in effect, offered as a form of “rescue therapy.”

This report describes the effect of sDHD on the different types of blood accesses in our study over a 39-month period.

### Materials and methods

#### Patient selection

The goal of participant recruitment was to have approximately 12 – 15 patients on sDHD at any time. All patients receiving in-center or home HD through El Camino Dialysis Services (approximately 400 patients) were screened for medical indications for sDHD. Potential study patients were advised of the benefits and risks of sDHD, and asked to commit to no less than 3 months on the study. The study protocol was evaluated and approved by the Institutional Review Board at El Camino Hospital. Written informed consent was obtained from patients prior to enrollment in the study.

Criteria for patient selection included three or four times per week, in-center or home HD for at least 3 months; willingness to reuse dialyzers if in-center; adequate blood access; compliance with treatment protocols; and having an appropriate indication for daily HD.

Initially, we selected patients based on medical justification for converting to sDHD, such as inability to tolerate the interdialytic interval (fluid overload), inability to tolerate the prescribed dialysis time (anxiety or physical discomfort with prolonged sitting), inability to control blood pressure, or malnutrition with failure to thrive. We later allowed a few patients to enroll for two nonmedical reasons, the desire to

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improve general well-being, and the desire to improve the dialysis schedule for work or family.

#### *Study protocol*

This was a prospective sequential study, with each patient serving as his/her own historical control. For patients adequately dialyzed three times per week, the weekly dialysis time was kept the same but was divided equally into six treatments per week. All other aspects of treatment were unchanged, such as dialyzer type, blood and dialysate flow rates, and adherence to dialysis unit protocols, as well as clinical management by their own attending nephrologist.

The minimum prescribed Kt/V on sDHD was 0.66 per treatment, or an aggregate value of 3.96 per week. The minimum delivered Kt/V on sDHD was 0.60 per treatment, or an aggregate value of 3.60 per week.

The following baseline data were gathered on each patient at the time of enrollment into the study: the number of admissions and hospitalization days for the 12 months prior to starting sDHD; the blood access history, especially detailed for the 12 months prior to starting sDHD; baseline Kidney Disease Quality of Life (KDQOL) questionnaire, version 1.3; and laboratory data for the 3 months prior to starting sDHD. The blood access history prior to sDHD was obtained by retrospective review of the patient's dialysis center chart, hospital records, and the outpatient clinic or physician office chart. Usage of accesses and transitions from one access to another were obtained from dialysis center charts and from outpatient clinic or physician office charts.

After starting sDHD, clinical and laboratory parameters were monitored monthly. The KDQOL was readministered at 3 months, then at annual intervals. Hospitalization and medical events were monitored. Cost data were collected annually.

All access problems occurring on sDHD were monitored and analyzed quarterly. Access problems were categorized by access type, type of problem, anatomical location of problem, date, and months of access use. Constant site or buttonhole method of venipuncture was not used in any of the patients.

#### *Statistical analysis*

Values are expressed as mean  $\pm$ SD. Student's paired *t*-test was used for comparison of means. A *p* value of less than 0.05 was considered statistically significant and a *p* value of less than 0.01 was considered highly significant.

#### **Results**

Over a 39-month period we enrolled 30 patients, for a cumulative observation time of 388 patient-months. There were 19 males and 11 females. Average age was  $57 \pm 16$  years. Causes of end-stage renal disease (ESRD) were diabetes mellitus type I or II ( $n = 7$ ), glomerulonephritis ( $n = 8$ ), hypertension ( $n = 6$ ), hereditary nephritis ( $n = 2$ ), and other

( $n = 7$ ). Patients had an average of  $3.8 \pm 1.3$  major comorbid conditions in addition to ESRD. Reasons for starting sDHD were inability to tolerate the interdialytic interval ( $n = 13$ ), inability to tolerate the prescribed dialysis time ( $n = 3$ ), inability to control blood pressure ( $n = 1$ ), malnutrition with failure to thrive ( $n = 8$ ), the desire to improve general well-being ( $n = 4$ ), and the desire to improve the dialysis schedule for work or family ( $n = 1$ ).

#### *Patient course*

Weekly conventional HD times ( $3.7 \pm 0.6$  hours, three times weekly) were divided into six sDHD treatments, each  $1.9 \pm 0.3$  hours. Weekly aggregate Kt/V remained unchanged. Thirty-patients were followed on sDHD for 388 patient-months: 9 patients died after  $4.2 \pm 6.7$  months, 3 were transplanted at  $5.4 \pm 2.2$  months, 3 were disenrolled at  $9.3 \pm 10.5$  months, and 15 remain on sDHD at  $20.4 \pm 14.1$  months. None of the disenrolled patients did so to voluntarily return to conventional HD (1 disenrolled for psychiatric decompensation, 1 switched to peritoneal dialysis because of recurrent blood access infections that antedated sDHD, and 1 moved out of the area).

Clinical course [1] and economic outcomes [8] have been reported elsewhere.

#### *Pre-DHD access outcomes*

All pre-sDHD or post-sDHD blood access events were categorized according to access problem and access type. In the 12 months prior to starting sDHD, 30 patients had 27 access problems in 40 different blood accesses, as shown in Table I. There are only 28.07 access-years for the 12 months pre-DHD because 3 patients were not on HD for a full 12 months.

Eight arteriovenous fistulas were used for 5.25 access-years with one problem, a stenosis in the outflowing basilic vein, distant from any venipuncture site, that required a saphenous vein interposition graft. Arteriovenous fistula problems pre-sDHD were 0.19 per access-year.

Nine polytetrafluoroethylene (PTFE) ABG accesses were used for 6.83 access years with 13 problems. There were 7 thrombectomies with surgical thrombectomy with revision ( $n = 4$ ) or percutaneous transluminal thrombolysis with angioplasty ( $n = 3$ ), 3 elective surgical revisions, and 3 elective percutaneous transluminal angioplasty (PCTA) procedures without thromboses. All the revisions and PCTAs were performed at the venous anastomosis. Polytetrafluoroethylene problems were 1.90 per access-year.

Fifteen bovine ABGs were used for 14.08 access-years, with 8 problems. There was one incision site infection after the access was used, requiring access removal; one thrombosis (graft lost); two thromboses, one with surgical revision and one with percutaneous thrombolysis and PTCA; two elective surgical revisions (one for stenoses in the body of the graft at venipuncture sites, the other at venous anastomosis); one elective PTCA; and one removal for steal syndrome. Only

TABLE I All access problems pre- and on six-times-weekly (daily) hemodialysis (sDHD), excluding incisional infections or failures that occurred before first use. There were no statistical differences between problems with any access type pre-DHD compared with on-sDHD.

Access type	12 Months prior to sDHD				Duration on sDHD			
	n	Access-years	Problems n	/Access-year	n	Access-years	Problems n	/Access-year
Fistulas	8	5.25	1	0.19	8	7.73	1	0.13
PTFE	9	6.83	13	1.90	8	11.54	16	1.39
Bovine	15	14.08	8	0.57	15	13.35	13	0.97
PC	6	1.83	5	2.73	7	1.92	1	0.52
TC	2	0.08	0	0.00	3	0.08	0	0.00
Total	40	28.07	27	0.96	41	34.44	31	0.90

PTFE = polytetrafluoroethylene graft; PC = permanent catheter; TC = temporary catheter.

one of these problems was clearly related to venipuncture sites. Bovine problems were 0.57 per access-year.

Six PC accesses were used for 1.83 access-years, with 5 problems. There were three catheter occlusions requiring stripping, one catheter sepsis, and one nonfunctioning catheter requiring removal. Permanent catheter problems occurred at 2.73 per access-year.

There were two temporary catheter (TC) accesses used for 1 month, with no problems.

*sDHD access problems*

After starting sDHD, 30 patients had 41 different blood accesses. There were 31 access problems, occurring over 34.44 access-years. There are more access-years than patient-years on sDHD as some patients had more than one access type at one time.

Eight AVFs were used for 7.73 access-years with one problem, a stenosis at the venous anastomosis of the previously placed saphenous vein interposition graft, distant from any venipuncture sites. A bovine segment was then used as a new interposition graft in this case. Arteriovenous fistula problems on sDHD were 0.13 per access-year.

Eight PTFE ABGs were used for 11.54 access-years, with 16 PTFE problems. There were 6 surgical thrombectomies, with 5 of the problems at the venous anastomosis, and 1 in the body of the graft; 3 elective surgical revisions and 3 elective PCTAs without thromboses; 3 thromboses with graft loss; and 1 sepsis due to graft infection. Rate of PTFE problems on sDHD was 1.39 per access-year.

Fifteen bovine ABGs were used for 13.35 access-years with 13 problems: 3 thromboses; 5 thromboses with 2 surgical revisions and 3 percutaneous thrombolyses with PTCA; 1 elective surgical revision; 3 elective PTCAs (1 in the body of the graft, 2 at venous anastomoses); and 1 aneurysm in the body of the graft, requiring interposition graft. Post-DHD bovine problems were 0.97 per access-year.

Seven PCs were used for 1.92 access-years, with 1 problem, catheter sepsis, treated with antibiotics only, an incidence of 0.52 per access-year.

There were three TCs used for 1 month with no problems.

**Discussion**

Daily HD is generally defined as five to six treatments per week, and therefore requires up to twice the number of times that the blood must be accessed. For all subcutaneous accesses, such as fistulas, grafts or implanted, ported central catheters, up to twice the number of venipunctures are necessary, with increased trauma to the skin and vessel. For transcutaneous tunneled or TCs there are that many more openings of the closed system, increasing opportunities for infection and wear and tear on the catheter parts.

Blood access survival and complications are understandably major concerns with DHD. It is because of these concerns that some of the pioneers of sDHD used single-needle techniques [2,3]. Contrary to these initial fears, however, recent reports describe better blood access outcomes with sDHD compared with conventional HD [2,4,5]. There has been interesting speculation why this may be the case. Some have attributed it to better hemodynamics from improved blood pressure control [6]. Others have raised the possibility of improved hemostasis with decreased thrombopathy or hematoma formation at the puncture site [9,10]. Reduced homocysteine levels have also been reported with sDHD and considered a reason for decreased graft clotting [11].

Twardowski reviewed this subject recently [10]. His conclusion was that AVF survival appears superior with sDHD, but that there is insufficient information on ABG or PC survival and complications with DHD.

Pierratos has since reported improved PC function with nocturnal DHD [7], speculating that daily heparin might have a beneficial effect. Lockridge recently confirmed this finding from his cohort of nocturnal DHD patients using PCs as well [12].

Our study describes outcomes of several types of blood accesses with sDHD. With the exception of one short-term (8-week) study [13], this is the first long-term comparative study of artificial bridge grafts. Sixty percent of all blood accesses in our study were ABGs, with about twice as many

of bovine material as PTFE. There was no difference in access problems for any of the access types comparing pre-sDHD with sDHD complications.

There were many methodological questions in analyzing blood access complications. The first was whether to compare all access problems. While we counted all access problems in our study, we chose not to include in our comparison in Table I those accesses that failed or developed a complication before first use. These problems definitely were not related to use. We included all other problems, including categories of access problems not necessarily attributable to use, such as accesses removed for steal syndrome or ischemic neuropathy, or the complications or failures that result from stenoses of the venous anastomosis or outflow vein proximal to any venipuncture sites.

Another methodological problem we encountered was how to count access-years in 1 patient whose access had two types of material in it. This patient had a radiocephalic fistula that developed a long area of stenosis in the upper arm where there had been no venipunctures. After this portion of the AVF was replaced with a bovine interposition graft, he had six subsequent interventions due to recurrent stenoses at the outflow of the bovine segment (an area that had never been used for venipuncture). We counted these as bovine-related problems because the problems were clearly related to the bovine outflow. However, the actual venipuncture sites were in his native cephalic vein, which was at risk of developing stenoses, aneurysms, or infections throughout the same period of time. In this patient, we accrued access times for both materials as if he had two different accesses, since both access types were at risk.

Comparing all access problems in our study, including those that failed before first use, would have added two additional bovine problems to the pre-DHD period and two bovine problems to the sDHD period. This would have increased the bovine problems per access-year to 0.71 pre-DHD and 1.12 sDHD. The total problems per access-year would be 1.03 pre-DHD and 0.96 sDHD, still not significantly different.

Table II presents only those access problems clearly related to use. These include only aneurysms, pseudoaneurysms, or stenoses in the part of the AVF or ABG that was punctured; infections in puncture or tape areas that required any antibiotic; mechanical failure of a catheter; and any catheter infection that required antibiotic treatment, whether sepsis or serious tunnel or exit-site infection. We excluded all problems not definitely related to use, such as venous outflow stenoses, the most common cause of graft failure. We also excluded steal syndromes and PC strippings, as well as the access failures occurring before first use.

What is interesting in Table II is how few problems are definitely related to venipuncture of blood accesses. It seems the majority are due to factors other than venipuncture, such as the body's reaction to high pressure and flow in a venous system designed for low flow and pressure, or to the presence of foreign material. It may be that those factors are far more important than the trauma of venipuncture, and that increased access use will not result in significantly increased blood access complication rates.

**Conclusions**

We conclude that sDHD does not appear to have an adverse effect on blood accesses, including artificial grafts and catheters, and that blood access problems should not be the major stumbling block to the widespread adoption of more frequent hemodialysis.

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TABLE II All access problems pre- and on six-times-weekly (daily) hemodialysis (sDHD) definitely related to frequent use. Included are all aneurysms, pseudoaneurysms, or stenoses in the part of the arteriovenous fistula or arteriovenous bridge graft that was punctured; infections in puncture or tape areas that required any antibiotic; mechanical failure of a catheter; catheter sepsis or serious exit-site infection. Excluded are steal syndromes, incisional infections, and failures that occurred before first use; thromboses or procedures resulting from stenoses at the venous anastomosis; and fibrin sheath stripping of tunneled catheters.

Access type	12 months prior to sDHD				Duration on sDHD			
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Fistulas	8	5.25	0	0.00	6	7.73	0	0.00
PTFE	9	6.83	0	0.00	10	11.50	2	0.17
Bovine	15	14.08	2	0.14	14	11.08	2	0.18
PC	6	1.83	1	0.55	7	1.92	1	0.52
TC	2	0.08	0	0.00	3	0.08	0	0.00
Total	40	28.07	3	0.11	40	32.31	5	0.15

PTFE = polytetrafluoroethylene graft; PC = permanent catheter; TC = temporary catheter.

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