Hemodialysis Access-Induced Distal Ischemia (HAIDI)

Diagnosis and surgical management

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CHAPTER 1

Introduction, aims and outline

INTRODUCTION

If a patient progressively suffers from end-stage renal disease, hemodialysis is life saving. Hemodialysis includes repeated cannulation of vascular structures. The patient's blood is directed towards an artificial kidney, cleared of waste metabolites and again shunted back into the patient's vascular system. This process ideally requires a large superficial vein with enough blood flow (> 300-600 ml/min) (1). In the normal situation such veins do not exist.

Creation of a connection between an artery and a vein (arteriovenous fistula, AVF) will lead to arterialization of a neighbouring venous network. Superficial veins will enlarge and allow repeated cannulations. Several types of AVF's have been used since its introduction in the mid 1960's. European and American guidelines promote a radio-cephalic AVF located at the wrist as a first choice access, and a brachio-cephalic elbow AVF as a second choice (1-3). The third option is transposition of the basilic vein in the upper arm. Prosthetic arteriovenous bridge grafts perform suboptimal on the long term and have lost popularity (4).

Various complications associated with an autogenous AVF may occur including immediate occlusion, non-maturation, inflow or outflow stenosis, infection, spontaneous bleeding, cardiac overload or distal hypoperfusion. Fortunately, most AVF's do not compromise distal limb perfusion. However, a small group of patients develops ischemia of distal tissues (5). Prolonged severe hypoperfusion may result in loss of hand function and tissue necrosis in about 1% of hemodialysis patients necessitating amputation of fingers, hand or even a forearm (6,7). The term 'steal' is commonly used to describe the phenomenon of distal ischemia in the presence of an AVF.

'Steal' and hemodialysis

Most authors use the term 'steal' when referring to hemodialysis access-related hand ischemia (8-15). The term steal suggests that ischemia is due to 'blood that is stolen' from distal parts of an extremity wherein this access has been constructed. However, steal and access-related distal ischemia are not identical. On the contrary, several observations argue against a relation between steal and distal ischemia.

Firstly, physiological blood flow measured in a resting axillary artery approximates 200 ml/min (16). Effective dialysis requires 250 to 300 ml/min blood flow through the artificial kidney, volumes that should minimally be generated by the access. A 200 ml/min arm flow can impossibly yield such high access flows on the short term. The term 'steal' to describe postoperative hand ischemia immediately following insertion of an arteriovenous fistula is under these circumstances incorrect.

Secondly, 'steal' in vascular surgery is used to describe reversal of flow in an artery, i.e. in a vertebral artery ('subclavian steal syndrome'). Reversal of mean arterial flow in this artery will not inevitably lead to locoregional (cerebral) ischemia. Only when a

compensatory increase of cerebropetal flow by way of collateral arteries is inadequate, symptoms of cerebral hypoxia may arise (17). The same principle applies to flow reversal in arm arteries including a distal brachial artery (for brachio-cephalic and brachio-basilic AVF's) or for the distal radial artery (radio-cephalic AVF).
Thirdly, reversal of flow in segments distal to an AVF is almost always (73-91%) observed following routine access insertion (18-20). As only a minority of these patients eventually develop hand ischemia, reversal of flow is obviously not a requisite for distal ischemia. The term 'steal' in relation to ischemia following AVF creation is misleading. Analogous to peripheral arterial obstructive disease (PAOD), AVF-related ischemia is probably caused by the combined hypotensive effects of a high flow through relatively stiff arterial conduits coupled to a low resistance AVF (12,17).
In this thesis, we propose to delete the confusing term hemodialysis associated 'steal' but instead to use the term HAIDI (hemodialysis access-induced distal ischemia). HAIDI is defined as a syndrome associated with tissue ischemia that develops in portions of extremities distal to an AVF that is used for hemodialysis. The present thesis will focus on diagnosis and surgical management of HAIDI.

GENERAL AIM OF THIS THESIS

To study diagnosis and management of chronic HAIDI in an average hemodialysis population.

SPECIFIC AIMS OF THE THESIS

1. To qualify and quantify symptoms of chronic HAIDI in a general dialysis population.
2. To perform a literature study on the efficacy of a surgical technique termed banding for HAIDI.
3. To identify clinical parameters that may guide banding in patients requiring surgery for chronic HAIDI.
4. To describe the short and long term efficacy of banding in HAIDI patients.
5. To study the effect of artificial kidney flow on systemic blood pressure and the finger's temperature and finger pressure in patients with HAIDI.

OUTLINE OF THE THESIS

Symptoms and signs of severe HAIDI in patients requiring surgery are well defined. However, the incidence of mild to moderate HAIDI in an average hemodialysis population is unknown. Using an 'ischemic questionnaire' in two different populations on chronic hemodialysis, incidence, frequency and severity of HAIDI associated with 3 types of AVF's are reported in **chapter 2**.
Some patients with HAIDI may benefit from an adaptation in the artificial kidney's flow level. The effects of manipulating the level of artificial kidney flow on finger pressure and finger temperature in patients with HAIDI are studied in **chapter 3**.
A surgical technique termed banding for the invasive treatment of chronic HAIDI is sceptisized because of high access occlusion rates. However, these dismal results may be due to the absence of intra-operative monitoring techniques guiding a banding procedure. A systematic literature search on efficacy of banding in relation to intra-operative monitoring techniques is reported in **chapter 4**.
It is unknown which physiological parameters are useful during these banding procedures. **Chapter 5** reports on alterations of various physiological parameters including access flow, venous saturation and digital finger pressures during stepwise banding in a group of patients requiring corrective banding.
The long term efficacy of banding is also unknown. Short term and long term efficacy of banding in patients with chronic HAIDI is reported in **chapter 6**.
The relation between type of AVF (autogenous, graft) and time of onset of HAIDI following a routine access construction is largely unknown. In a systematic literature overview in **chapter 7** the existence of such associations is analyzed.
Chapter 8 and 9 describe rare sequelae associated with chronic HAIDI. A successfully renal transplanted teenage girl with an elbow AVF demonstrates a hypotrophic access-side hand due to steal and an inflow stenosis (**chapter 8**). A second patient demonstrates multiple skin tumors in a severely ischemic HAIDI hand (**chapter 9**), possibly related to a chronic hypoxic state.
Banding is also used for the treatment of high flow AVF's (HFA). **Chapter 10** outlines several aspects of HFA and critically evaluates the banding procedure for this phenomenon.
Chapter 11 provides a summarizing discussion, conclusions and future directions. All studies are summarized in Dutch in **chapter 12**.

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CHAPTER 2

Steal in hemodialysis patients depends on type of vascular access

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ABSTRACT

Objectives

To study incidence and severity of steal phenomena in hemodialysis patients and to investigate possible methods for its detection.

Methods

A questionnaire was composed based on a literature search. A subgroup of patients having steal as identified by the questionnaire was studied using physical examination, arterial blood pressure, skin temperature, digital oxygenation, grip strength and plethysmography. Contralateral arms served as controls.

Results

A cold hand was present in 50% of the patients with a brachiocephalic (BC) arteriovenous fistula (AVF, n=28) compared to 25% of prosthetic forearm loops (loop, n=27) and 12% of the radiocephalic (RC, n=65, $p<0.05$) fistulas. Diabetics were at risk for steal ($p<0.001$). Intensity of steal was not related to magnitude of access flow. Digital skin temperatures and grip strength were lower in steal hands ($p<0.02$). Manual compression of the AVF normalised low digital pressures in steal hands (106±33 vs 154±25 mm Hg, $p<0.001$, contralateral side 155±21 mm Hg).

Conclusions

Mild to moderate steal symptoms are common in a hemodialysis patient. Individuals with a BC are at a higher risk for developing complaints associated with reduced hand circulation compared to patients with a RC or loop. Low finger pressures in the presence of steal symptoms are usually reversible in a hemodialysis access.

INTRODUCTION

Patients require an optimal dialysis access if kidney function falls below a critical value. If hemodialysis is unavoidable, an arteriovenous fistula (AVF) placed at the wrist (radiocephalic fistula, 'RC') is thought superior by most surgeons. Although some prefer an autogenous brachiocubital fistula (elbow, 'BC') as a second choice, others opt for an access positioned at the forearm using a prosthetic graft loop fistula ('loop') (1).
Functioning of any type of AVF is largely dependent on blood flow. Thrombosis and occlusion may occur if fistula flow drops below a minimal threshold value. In contrast, greatly augmented flows may lead to ischemia of the forearm and hand (2). In the latter situation, acral blood flow is directed towards the AVF leading to peripheral 'steal' phenomena (3). Steal is thought to occur more easily if a fistula is located on proximal portions of the upper extremity and its intensity may be related to blood flow through the arteriovenous anastomosis.
Subjective symptoms of steal are characterized by coldness, pain, cramps and altered sensibility. Frequency and intensity of mild and moderate steal are unknown. Incidence of severe steal possibly requiring corrective surgery is also not known but may range anywhere from 0.5 to 5% (4). In addition, an objective 'gold standard' method that clearly discriminates between presence or absence of ischemia in a hemodialysis arm has not been identified although low finger pressures may be associated with steal (5,6).
The present study has two aims. Firstly, to study incidence of steal phenomena in patient populations with three different dialysis accesses. Secondly, to investigate whether diagnostic tools are capable of detecting steal in hemodialysis patients reporting ischemic symptoms.

PATIENTS AND METHODS

A. Study population and questionnaire

The study was conducted between January 2003 and January 2004. Patients were recruited from two dialysis facilities (Veldhoven, hemodialysis capacity n=90, Maastricht n=67). Only patients receiving chronic hemodialysis (> 6 months) and having well-functioning dialysis accesses were eligible for the study (n=157). Patients were not studied if they refused (n=14), or displayed a cognitive (n=15) or language (n=8) handicap. The remainder of the patients (n=120) was informed on the nature of the study and consented to its specifics.
A search was conducted on literature related to steal in the presence of a dialysis fistula using standard computer searching strategies. These data were used to compose a questionnaire aimed at studying incidence and severity of steal symptomatology. Questionnaires were completed by patients themselves under close supervision of one of two dedicated nurses belonging to the access surveillance team.
Severity of steal was evaluated using a Visual Analog Scale (VAS, 0=no complaints, 10=maximum of complaints). Frequency of symptoms was measured with similar VAS-techniques (0=never, 10=always). The 'steal score' of each individual was calculated as the sum of coldness (severity (s) x frequency (f), pain (s x f), loss of sensibility (s x f), loss of strength (s x f) and cramps (s x f, see 'appendix' for details). This steal questionnaire was initially tested in a group of 25 patients. Their steal scores indicated that 14 individuals experienced symptoms of steal to a certain extent (mean steal score: 60 ± 10, range: 1 - 189) whereas 11 did not (steal score = 0). The questionnaire was completed by the entire study population (n=120) at a later stage of the study.
All arteriovenous fistulas were created using standard techniques. The RC fistulas were all end-(cephalic vein) to-side (radial artery) constructions. The BC group harboured 79% end- (Gracz vein) to-side (brachial artery), and 21% side-(Gracz vein) to-side (brachial artery) AVF's. All prosthetic loops were connected between the brachial artery and a neighbouring vein; none had tapered or expanded ends (6 mm, PTFE, Gore and Assoc., Flagstaff, USA).

B. Steal detection techniques

Results of the steal questionnaire obtained from the 25 patient pilot study indicated that 14 individuals subjectively experienced symptomatology possibly associated with the presence of steal. It was assumed that selected tools were capable of detecting steal in dialysis access arms in this subgroup. Measurements of the contralateral arm provided control values. All studies were performed just before the start of a dialysis session.
Physical examination of both arms and hands including inspection revealed if skin color was normal, or whether pallor or cyanosis were visible. Also the presence of trophic lesions (nails, loss of hair, muscle atrophy), ulcers or diminished capillary refill (>3 sec) was tabulated. Pulsations of both radial and ulnar arteries were scored (absent (0), weak (1), diminished (2) or normal (3)). Sensibility of the skin of the hand was tested using two point discrimination (sharp/soft) and was scored as normal (score = 2, all three tests were felt similar to the contralateral arm), diminished (1, at least one out of three tests was correctly sensed by the patient) or absent (0, no test was correctly counted by the patient). Skin temperatures of both dorsum and palm of the dialysis hand were compared with the contralateral side by the principal investigator (FvH) and subjectively scored as similar or colder.
Blood pressure of the contralateral brachial artery was determined with the patient in a sitting position. Bilateral measurements of systolic blood pressure in the radial and ulnar artery were performed using standard Doppler equipment (Dopplex, Huntleigh Diagnostics, Cardiff, UK). Skin temperature of various portions of the hand was measured using a digital thermometer (Genius First Temp, M 3000A, Sherwood Medical, Sussex, UK). The sensor was held in a 45 degree angle 1 cm above the skin, and measurements

were done of dorsal and palmar portions of the hand as well as the distal phalanx of the index finger. Also oxygen saturation of the index finger was measured using a standard saturation meter (Ohmeda Biox, 3700e, Pulse oximeter, Louisville, USA). Capillary bloodgas specimens were obtained from palmair portions of the index finger and analyzed using standard laboratory techniques (ABL700 FLEX, Radiometer, Copenhagen, Denmark). Grip strength of both hands was measured using hydraulic hand grip dynamometry (SH 5001, SAEHAN Corp, Korea). The patient was standing with the dynamometer in an extended arm. Subsequently, the arm was flexed 90 degrees while maximally squeezing the calipers. This exercise was repeated twice, and the best result was noted. Plethysmography was used to determine pressures of the index finger of both hands (VasoGuard Nicolet, 8 Mhz, Scimed Ltd, Bristol, UK), during manual compression of the venous portion of the AVF as well as during the open/normal situation. An inflatable cuff was wrapped around the proximal phalanx of the index finger and the sensor was positioned on the palmar side of the distal phalanx. The digital brachial index (DBI) was calculated as the ratio of finger pressure to systolic blood pressure. Access flow was measured in duplicate using the transonic flowmeter and expressed in ml/min (HD01, Transonic Systems Inc, New York, USA) (7).

STATISTICAL ANALYSIS

Data were expressed as mean ± sd (or sem). Differences between groups with respect to the steal questionnaire were determined using Chi-square tests. Access flows were compared using an univariate analysis of variance. Non-parametric tests (Kruskal-Wallis) were used to determine group differences in severity and frequency of steal. Paired T-tests or Wilcoxon signed rank tests were performed when appropriate. A $p<0.05$ was considered significant.

RESULTS

A. Steal questionnaire

The questionnaire was completed by 120 patients. More than half of this population harboured a RC (n=65), whereas approximately one quarter used a BC (n=28) or a prosthetic forearm loop (n=27) for hemodialysis. These three groups of patients were similar with respect to age, sex distribution, percentage of diabetes mellitus and access flow (table 1). Cold sensation was reported more frequently in the BC-group when compared to the RC-group. Also a trend was present for cramps to occur more frequently in the BC-group. The majority of BC-patients (79%) complained of at least one symptom of steal compared to the RC-group (38%) ($p<0.05$) or the loop-group (52%, figure 1). Severity and

frequency of steal symptomatology as measured by a VAS score are depicted in table 2. Type of access did not influence frequency and severity of reported steal. In other words, if steal was present, its symptomatology was not more pronounced in one type of access compared to another. These VAS scores also indicate that symptomatic patients in the three different populations very frequently experience cold sensation (range 6.4-7.7) of moderate severity (4.6-6.4). Symptomatic patients also frequently (5.1-6.6) suffer from pain of mild (3.7-3.8) intensity. Most patients experience cramps only now and then. In contrast, diminished strength was almost always present (6.8-7.8) in all of the symptomatic patients. Thirty-one patients reported a steal score of 0 (total absence of any symptom traditionally associated with steal). The remainder of the group (n=89) reported minor (score=1) to extremely severe symptomatology of steal (score=276).

	RC	BC	Loop	p
N	65	28	27	
Age (y)	66 ± 13	65 ± 14	69 ± 10	0.73 *
Male N (%)	42 (65)	15 (54)	11 (41)	0.10 *
Diabetes Mellitus N (%)	11 (17)	6 (21)	1 (4)	0.15 *
AVF flow (ml/min)	855 ± 466	1147 ± 724	1040 ± 409	0.86 ‡

Table 1 Characteristics of dialysis study population (n=120) that completed a steal questionnaire
**Chi-square, ‡ Univariate Analysis of Variance*

		RC (65)	BC (28)	Loop (27)	p
Cold sensation	N (%)	8 (12)	14a (50)	7 (26)	<0.001 *
	Severity	5.1 ± 3.1	6.4 ± 3.0	4.6 ± 3.5	0.36 †
	Frequency	6.4 ± 3.3	7.7 ± 2.7	7.6 ± 2.8	0.65 †
Pain	N (%)	11 (17)	9 (32)	9 (33)	0.13 *
	Severity	3.7 ± 2.0	3.8 ± 2.1	3.7 ± 2.1	0.96 †
	Frequency	5.6 ± 3.3	5.1 ± 1.9	6.6 ± 3.2	0.64 †
Cramps	N (%)	16 (25)	13 (46)	8 (30)	0.08 *
	Severity	3.2 ± 1.1	3.3 ± 0.9	3.4 ± 1.2	1.0 †
	Frequency	3.9 ± 1.3	4.1 ± 1.4	4.5 ± 1.7	0.8 †
Diminished sensibility	N (%)	16 (25)	11 (39)	7 (26)	0.34 *
	Severity	4.8 ± 2.6	5.3 ± 2.8	5.3 ± 3.4	0.92 †
	Frequency	7.0 ± 3.5	6.2 ± 3.4	5.1 ± 2.6	0.46 †
Diminished strength	N (%)	21 (32)	15 (54)	7 (26)	0.12 *
	Severity	5.0 ± 1.8	5.4 ± 1.9	5.6 ± 3.0	0.85 †
	Frequency	7.8 ± 2.6	6.8 ± 3.7b	7.4 ± 4.1	0.03 †
Minimal 1 complaint	N (%)	25 (38)	22c (79)	14 (52)	0.01 *

Table 2 Severity and frequency of steal reported by patients (N) with three different dialysis accesses (VAS, 0 (min) - 10 (max)
** Chi-square, † Kruskal Wallis, a: $p < 0.001$ versus RC , b: $p < 0.01$ versus RC, c: $p < 0.05$ versus RC*

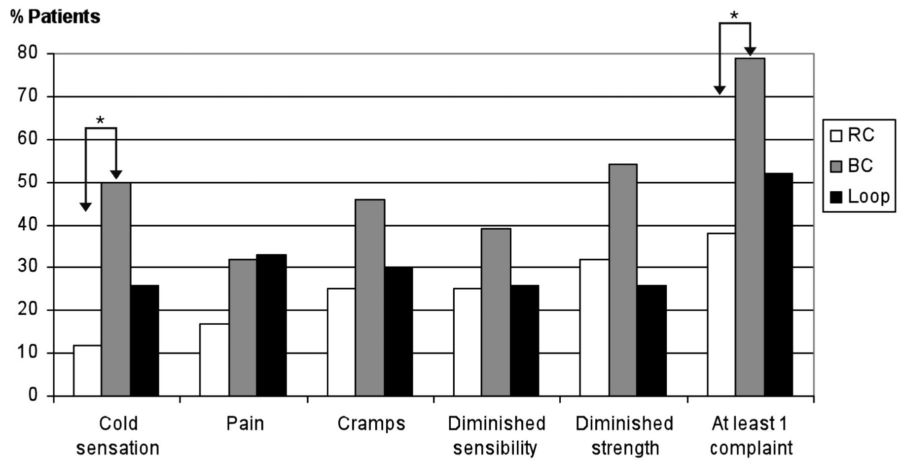

Figure 1 *Incidence of steal symptoms as identified by a steal questionnaire in 3 different groups of dialysis accesses (RC=65, BC=28, loop=27), *p<0.05*

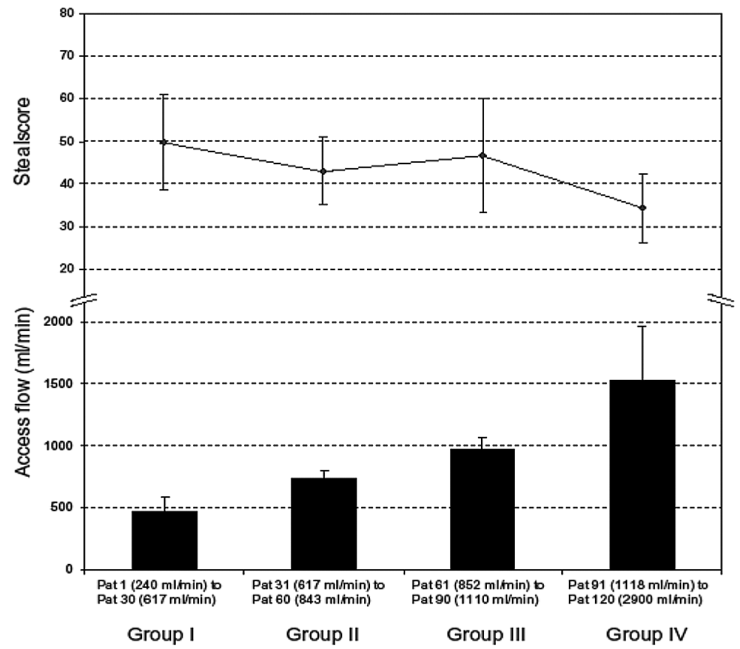

Figure 2 *Access flow and steal scores. High access flows were not associated with more intense steal symptomatology as identified by a questionnaire.*

The relationship between steal scores and access flow for all 120 patients is depicted in figure 2. Contrary to what one would expect, patients with high flows did not report more symptomatology associated with steal compared to patients with low flow accesses (p=0.30). However, diabetics (n=18) displayed higher steal scores compared to non-diabetics (85±20 vs 36±5, p<0.001).

B. Studies for detection of steal

A group of patients (n=14) was identified by the questionnaire and served as study group. Five individuals had a RC and 9 persons harboured a BC access. This group was not different from the remainder of the group that experienced steal as determined by the questionnaire with respect to age, gender, diabetes mellitus or access flow (table 3). It is therefore assumed that the results of measurements obtained from this group of 14 patients is representative of the entire group that reported symptomatology associated with steal (n=89). Results of physical examination are shown in table 4. Inspection revealed that pallor or cyanosis, trophic lesions or diminished capillary refill were frequently observed in the AVF-hand when compared to the contralateral side (13 vs 5). Pulsations of the radial artery were less pronounced on the AVF side compared to the healthy arm. Ulnar artery pulsations were decreased on either side, most probably due to its hidden position. Hand temperature, as determined subjectively by the main

	Steal (tested)	Steal (not tested)	No Steal	p
N	14	75	31	
Age (y)	68 ± 16	66 ± 13	66 ± 14	0.51
Male n (%)	9 (64)	39 (52)	19 (61)	0.40
Diabetes Mellitus n (%)	3 (21)	12 (16)	3 (10)	0.28
AVF Flow (ml/min)	1257 ± 773	936 ± 400	853 ± 526	0.12‡

Table 3 *Characteristics of subgroup of 14 steal patients that underwent test panel compared to remainder of steal group (n=75, not tested) and group without steal (n=31)*
Chi-square, ‡ Univariate Analysis of Variance

Number of patients (%)	AVF arm	Contralateral arm	p
Pallor/cyanosis	6 (43)	2 (14)	0.19
Trophic lesions	4 (29)	2 (14)	0.47
Ulcers	0 (0)	0 (0)	
Capillary refill (>3 sec)	3 (21)	1 (7)	0.59
Total	13 (93)	5 (36)	0.23

Table 4 *Hand inspection in a subgroup of patients on chronic dialysis (n=14) reporting steal*
Analysis by Chi-square

investigator, was significantly lower on the AVF-side compared to the contralateral hand (table 5, $p<0.01$).
Temperatures of the index finger of the AVF-hand were on average 1.0 °C lower compared to the contralateral side (table 6, $p<0.02$). Moreover, hand grip strength was approximately 20% lower in the dialysis hand (17.9±10.0 vs 22.2±11.4 kg, $p<0.001$). Finger pressures increased dramatically following compression of the venous portion of the AVF (open: 106±33 vs closed 154±25, $p<0.001$). The magnitude of change in finger pressure (in mm Hg) following AVF-compression and access flow (ml/min) were not related. Moreover, no inverse relation was present between absolute values of finger pressures (or DBI), and access flow.

	AVF arm	Contralateral arm	p
Radial artery (0-3)*	2.0 ± 1.2	2.9 ± 0.4	0.02
Ulnar artery (0-3)*	1.1 ± 1.3	1.6 ± 1.1	0.28
Diminished sensibility N (%)	2 (14)	0 (0)	0.16
Lower skin temperature N (%)	7 (50)	1 (7)	0.01

Table 5 Palpation of the dialysis hand in patients (n=14) reporting steal
Wilcoxon Signed Rank Test (0=absent, 3=normal, see material and methods for explanation)

	AVF arm	Contralateral arm	p
Blood pressure (mm Hg)			
Brachial artery, systolic	not measured	155 ± 16	
Brachial artery, diastolic	not measured	77 ± 13	
Radial artery systolic (Doppler)	150 ± 59	152 ± 28	0.78
Ulnar artery systolic (Doppler)	162 ± 36	152 ± 29	0.04
Temperature hand (°C)			
Dorsum	32.5 ± 1.4	32.1 ± 1.6	0.40
Palm	34.3 ± 1.8	34.1 ± 1.4	0.57
Top dig II	30.7 ± 2.7	31.7 ± 2.6	0.02
Oxygenation dig II			
Saturation (%)	97.3 ± 1.5	96.9 ± 1.1	0.29
pO2 (Capillary gas)	64.1 ± 12.4	67.3 ± 8.4	0.16
Strength (Kg)			
Hand grip	17.9 ± 10.0	22.2 ± 11.4	<0.001
Finger pressure dig II (mm Hg)			
Open AVF	106 ± 33	155 ± 20	<0.001
Closed AVF	154 ± 25a		
DBI	0.6 ± 0.3	0.9 ± 0.3	0.01

Table 6 Results of a test panel in patients (n=14) reporting steal
a: p < 0.001 versus open AVF, Paired Samples T-Test

A. GENERAL INFORMATION

1 Name, age, sex
2 Type of fistula
3 Date of (last) operation
4 Side
5 Left or right dominance

B. SPECIFIC INFORMATION

Cold sensations
1 Do you experience cold sensations in the fistula arm/hand (if not, go to question 6)?
2 Which location (lower arm/wrist/hand/fingers)?
3 Which finger(s)?
4 Severity of cold sensation (0= no cold sensation, 10= freezing cold)?
5 Frequency of cold sensation (0= never, 10= always)?

Minimal = 0, Max = 10 (severity) x 10 (frequency) = 100 points for cold sensation

Pain
6 Do you feel pain in the fistula arm/hand (if not, go to question 11)?
7 Which location (lower arm/wrist/hand/fingers)?
8 Which finger(s)?
9 Severity of pain (0 = no pain,10 = unbarable)?
10 Frequency of pain (0 = never, 10 = always)?

Minimal = 0, Max = 10 x 10 = 100 points for pain

Sensibility
11 Is diminished or altered sensibility present in the fistula arm/hand (if not, go to question 14)?
12 Severity of diminished sensibility (0 = normal sensation, 10 = total numbness)?
13 Frequency of diminished sensibility (0 = never, 10 = always)?

Minimal = 0, Max = 10 x 10 = 100 points for altered sensibility

Strength
14 Do you experience diminished strength in the fistula arm/hand (if not, go to question 17)?
15 Severity of diminished strength (0 = normal strength, 10 = total weakness)?
16 Frequency of diminished strength (0 = never, 10 = always)?

Minimal = 0, Max = 10 x 10 = 100 points for strength

Cramps
17 Do you suffer from cramps in the fistula arm/hand (if not, go to question 20)?
18 Severity of cramps (0= no cramps, 10 = spasms)?
19 Frequency of cramps (0 = never, 10 = always)?

Minimal = 0, Max = 10 x 10 = 100 points for cramps
Maximal Steal Score = 500 points

Appendix-Steal Questionnaire

DISCUSSION

Severe hand ischemia due to steal in the presence of a hemodialysis fistula is considered rare and seldomly requires corrective surgery. The incidence of either severe or mild steal is unknown, since few studies have solely focused on the occurrence of steal phenomena in dialysis patients. Consequently, it is also unclear which factors trigger its onset. In the first month following construction, most AVF's show a reversed direction of blood flow in the distal radial artery. This initial hand hypoperfusion may not be noticed by the patient and usually improves over time (8-11). If however frank steal symptoms emerge later on, intensity may become more pronounced over time requiring intensive follow-up (11,12). Interestingly, reversed blood flow in the radial artery may also be present in mature AVF's as demonstrated by Bussel (3). In contrast, reversed flow in proximal portions of the arterial vasculature such as the brachial artery has not been documented.

Daily practice has unveiled some characteristics of access-induced steal. The incidence of 'late' steal is known to depend on the location of the AVF. For instance, clinically significant steal associated with the presence of a RC fistula is reported in 1.8% of the patients. Moreover, steal in forearm loops and BC fistulas may occur in up to 6% of the population and between 10 - 25%, respectively (8,13-15). The onset of steal is thought to occur more readily in fistulas with large anastomoses and high flows (16). Generalized arteriosclerotic disease, secondary hyperparathyroidism, carpal tunnel syndrome (17) and neuropathy associated with uremia or diabetes may exaggerate or mimic steal symptomatology (18-20). For instance, some authors reported that the majority of patients with steal symptoms of the hand following creation of an AVF were diabetic (9,21). It is unclear whether these comorbid conditions worsen hand ischemia, or only add to its symptomatology since most studies used no objective tools for the measurement of digital hypoxia. Also in the present study a relationship between diabetes and intensity of steal was observed.

This study systematically investigated incidence of symptomatology traditionally associated with steal in hemodialysis using a novel questionnaire. This study is the first that compares incidence of steal in three different populations of arm accesses. A questionnaire was composed on the basis of an extensive literature search and included questions on incidence, intensity and frequency of steal symptoms. A stable population on chronic dialysis was studied, and a subgroup who reported steal in the questionnaire was selected and underwent measurements using a set of investigational tools. Half of the study population had a RC, whereas one quarter harboured loops and BC's, respectively. These populations were similar with respect to age, gender, % diabetes and access flow. The results of the questionnaire demonstrated that mild and moderate steal symptoms in each population are experienced on a much larger scale than previously thought. For instance, the RC-group reported steal symptoms to some degree in a frequency ranging from 12% (cold hand) to 25% (pain, cramps, diminished sensibility and weakness). Moreover, the BC-fistula appeared to generate ample steal phenomena. Half of the BC-population complained of a crampy, weak and cold hand. The incidence of steal associated with the presence of a forearm loop was in general similar to the RC-group. The questionnaire also investigated frequency and severity of symptoms in patients that reported steal. If a patient indeed suffers from steal, intensity is not different among the three dialysis populations. In other words, type of AVF does not determine intensity of steal symptomatology. Interestingly, pain was reported of mild intensity (mean VAS was 3.7 on a 0-10 scale). In contrast, weakness was moderate (VAS up to 5.6) and very frequent (7.8).

What is the clinical relevance of these findings? DOQI advocates the construction of a BC as an alternative second choice fistula. It must be realised that this form of dialysis

access is potentially associated with ample steal symptoms. Therefore, if several risk factors for steal are present in the predialysis situation (diabetes, generalized arteriosclerotic disease, hyperparathyroidism), particularly in the presence of low finger pressures, one may consider implanting a prosthetic forearm loop fistula.

A second aim of the study was to perform a pilot study with a set of investigational tools aimed at objectively detecting steal in hemodialysis patients. The questionnaire identified a representative subgroup of 14 patients that experienced steal. Their contralateral arm was used for obtaining control values, thus excluding potential comorbidity as a confounding factor. Simple physical examination revealed the presence of pallor, cyanosis and prolonged capillary refill in some steal hands. Moreover, pulsations of radial arteries were significantly less prominent on the steal wrist when compared to the contralateral side. This phenomenon may be related to reversed blood flow and a lower vascular peripheral resistance. Although one would expect lower systolic blood pressures in the radial artery, no significant difference was observed compared to pressures on the contralateral side. Testing skin temperature of the dialysis hand as performed by palpation by the principal investigator is considered a rather subjective investigation with obvious limitations. Nevertheless, in half of the patients ($n=7$) the steal hand was judged cooler compared to only one cold hand on the other side ($p<0.01$). Therefore, less pronounced arterial pulsations combined with a cooler hand are simple (although subjective) observations and may aid in the diagnosis 'steal' in the presence of an AVF.

Although physical examination is a first and probably subjective step in determining steal in the presence of an AVF, a physician would be greatly aided by an objective test that was able to discriminate between presence or absence of steal. In this study temperatures of both dorsum and palm were not different, but the temperature of the index finger was significantly lower on the dialysis hand. It may well be that this portion of the hand, because of its distal location, is prone to exhibit the consequences of diminished blood flow in an early phase. Capillary blood gas measurements appeared not to help in establishing the diagnosis. Pulse oximetry is reported an useful diagnostic tool for evaluating oxygenation status and cyanosis distal to an AVF (22,23). However, in the present study oxygen saturation as measured with oximetry was not discriminative. In concert with others, a lower hand grip strength in the dialysis arm was found. This finding supports data used by DOQI to instruct patients not to carry heavy weights with their dialysis arm (1). Grip strength is known to fall with increasing age in a nonlinear way. Lower limits of acceptable grip strength are defined as 85% of the normal strength adjusted for age and sex (24). All steal patients who performed grip strength measurements had values well below this 85% threshold (mean: $53 \pm 5\%$). Surprisingly, also in the non-dialysis hand low values were observed (mean: $68 \pm 6\%$). Only 4 patients had values equal or more than the 85% lower limit ($p<0.01$). These grip strength measurements indicate that chronic dialysis leads to considerable loss of muscle function in general, and these phenomena may intensify in the presence of steal.

Most authors argue that presence of steal and access flow are related in a direct fashion. The present study does not find this relationship. On the contrary, patients with the highest steal score as determined by the questionnaire showed a trend towards lower access flows when compared to patients that displayed a steal score of nil. Several factors may contribute to explaining this discrepancy. A direct relationship may only be true in high output fistulae but not in medium or small ones as present in our study. Moreover, sensations traditionally associated with the presence of steal (cold feelings, cramps etc) may be caused by a spectrum of factors in which ischemia only plays a limited role. The present study has not looked into the contribution of other factors such as uremic neuropathy or hyperparathyroidism. However, diabetics appeared at risk for steal as demonstrated by other investigators.

Photoplethysmography may be the only investigational tool that is thought to have potential in diagnosing steal in hemodialysis. A ratio of finger to arm blood pressure (DBI, digital-brachial index) of 0.6 is reported as a cut-off point, with a sensitivity for steal of 100%, and a specificity of 63- 76% (5,6). The mean DBI value in our group of patients was 0.6, but a range of 0.44 to 1.08 indicates that even a patient with a high DBI may experience steal. Finger pressure measurements with and without external compression of the AVF revealed that 'closing' of the fistula resulted in a 45% increase in finger pressure (106±33 mm Hg vs 154±25 mm Hg) and returned to normal levels similar to the other side (155±20 mm Hg). These results show that each of these AVF´s obviously does steal, as determined by photoplethysmograpic measurements. Moreover, low finger pressures in patients who subjectively report steal return to normal values following closure of the AVF. Steal in these patients is therefore not fixed but reversible and possibly responsive to corrective surgery if ever required (4).

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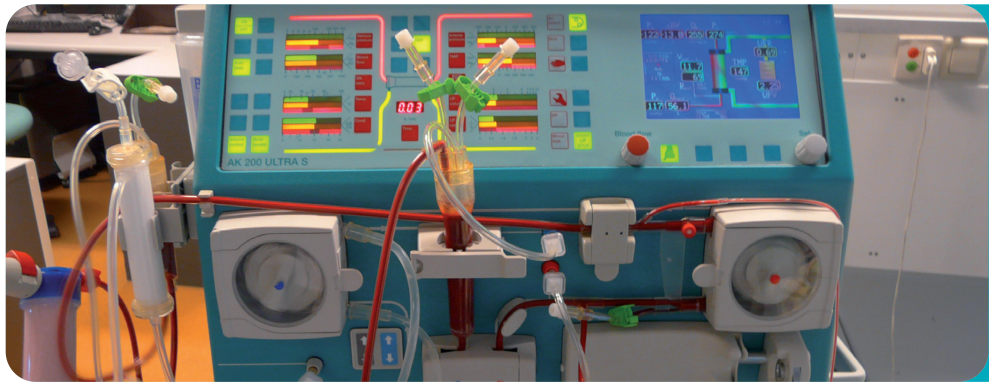
CHAPTER 3



Hemodialysis decreases finger pressures independent of artificial kidney blood flow

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ABSTRACT

Background

During hemodialysis, some patients experience intensification of symptoms of hemodialysis access-induced distal ischemia (HAIDI). Aim of this study is to compare the effects of two different regimens of arterial blood flow in patients with an arteriovenous fistula (AVF).

Methods

A questionnaire identified ten patients that subjectively experienced ischemic symptoms during hemodialysis. Systolic blood pressure (SBP), heart rate, finger pressure (Pdig), finger temperature (Tdig), oxygen saturation and ischemic scores were monitored during two different arterial blood flow dialysis sessions.

Results

Prior to dialysis, Pdig and Tdig of the AVF hand were significantly lower compared to the other hand. Hemodialysis induced a drop of Pdig in both hands. All changes in Pdig occurred independent of the artificial kidney's blood flow level.

Conclusions

Systemic hypotension following onset of hemodialysis further intensifies an already diminished hand perfusion. Measures preventing dialytic hypotension will likely attenuate symptoms associated with HAIDI during hemodialysis.

INTRODUCTION

Up to 5% of patients with an autogenous arterio-venous elbow fistula (AVF) suffer from severe hemodialysis access-induced distal ischemia (HAIDI) of the ipsilateral hand (1). They report unacceptable coolness, cramps, diminished strength or even rest pain. A recent study in an average hemodialysis population found that moderate HAIDI associated with radiocephalic and brachiocephalic AVF's was present in even higher percentages (38% and 78%, respectively) (2). Symptomatic individuals that were evaluated by a panel of tests demonstrated low hand skin temperatures (T_{dig}) and diminished digital pressures (P_{dig}) compared to the contralateral hand. Manual compression of the AVF usually reverses digital hypotension indicating that HAIDI is not fixed and likely amendable to treatment (2).
Although most HAIDI patients report symptoms in resting conditions, some may experience more intense distal ischemia during a hemodialysis session. Conversely, these individuals incidentally report attenuated symptoms following manipulation of the artificial kidney's blood flow. It is unclear if increased severity of HAIDI during dialysis is associated with 'dialysis induced hypotension', a frequently occurring systemic response (15-50%) including nausea, vomiting, headache and muscle cramps (3,4).
Perfusion of both hands has not often been studied during hemodialysis. A few studies observed altered arterial oxygen saturation on the AVF side (5-7). However, ischemic symptoms reported by a patient as well as P_{dig} and T_{dig} have not been studied simultaneously during a dialysis session.
Aim of the present investigation is to study the effects of altered blood flow on ischemic symptoms, digital perfusion and Tdig in hemodialysis patients. We hypothesized that P_{dig} and T_{dig} during a hemodialysis session are dependent on the level of the artificial kidney's blood flow.

PATIENTS AND METHODS

This pilot study was performed in January and February 2007 in the Maxima Medical Center (MMC) in Veldhoven, The Netherlands. The MMC is a 835-bed general hospital with a regional dialysis center accommodating approximately 130 chronic dialysis patients, 100 of them on intermittent hemodialysis (HD).
During resting conditions, incidence of symptoms consistent with HAIDI in this HD population was quantified by a previous published questionnaire (2). This questionnaire attains scores on five cardinal symptoms associated with HAIDI (coolness, pain, cramps, diminished sensibility and strength). By using a visual analogue scale system (VAS), severity (minimal 0, maximal 10) and frequency (minimal 0, maximal 10) of each of these symptoms is separately indicated by the patient supervised by a dialysis nurse.

Scores for each symptom range from 0 (0x0) to 100 (10x10) and are added to a total score (minimal 0, maximal 500). Validation in two groups of HD patients (n=120) indicated that an average population score varies between 35 and 50 points (2). A recent study in patients with unacceptable HAIDI demonstrated that successful surgery reduced ischemic scores from 153±33 to 42±15 (8).
For the purpose of the present study, the same questionnaire was again used in our hemodialysis center. A subpopulation of patients was identified that occasionally reported intensification of symptoms during dialysis (n=15). These individuals were asked to participate in this pilot study and consented to its nature and specifics.

Measurement protocol during a dialysis session

Measurements including ischemic symptom score, blood pressure, heart rate (HR, beats/min), oxygen saturation, P_{dig} and T_{dig} of both index fingers were determined just prior to dialysis, after 60, 120, 180 min, and immediately after discontinuation (figure 1). Ischemic symptoms were scored by the patient supervised by the principal investigator (FvH) and were expressed in whole numbers (minimal 0 - maximal 500). Systolic and diastolic blood pressures (SBP, DBP, in mm Hg) of the contralateral brachial artery were determined using an inflatable upper arm cuff. Mean arterial pressure (MAP, mm Hg)

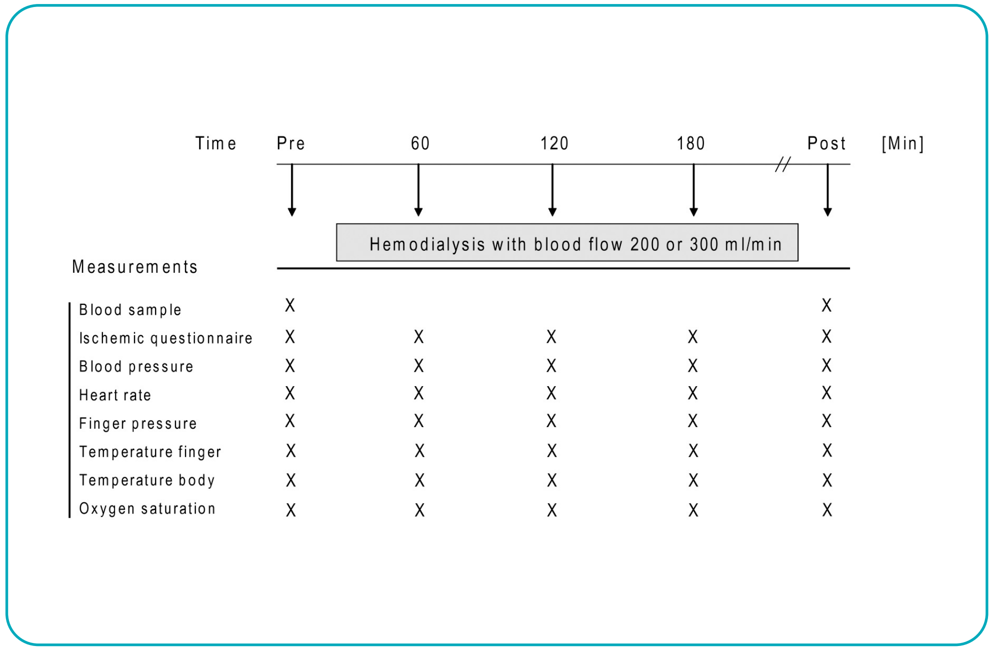

Figure 1 Study protocol

was calculated using the formula MAP = ((SBP - DBP) /3) + DBP. Oxygen saturation of the index finger (%) was measured using a standard saturation meter (Ohmeda Biox, 3700e, Pulse oximeter, Louisville, USA). P_{dig} of both hands (mm Hg) was performed using a plethysmographic technique (VasoGuard Nicolet, 8 Mhz, Scimed Ltd, Bristol, UK). An inflatable cuff was wrapped around the proximal phalanx of the index finger, and the sensor was positioned on the palmer side of the distal phalanx. The digital brachial index (DBI, normal 0.8-1.0) was calculated as the ratio of P_{dig} to SBP. T_{dig} of both index fingers (°C) was measured with a temperature sensor placed on volar parts of the distal phalanx (Fisher & Paykel Healthcare SAS, Courtaboueuf Cedex, France). The heating element was turned away from the patient's hand and did not influence readings. Body temperatures before and during dialysis were measured repetitively using an infrared tympanic thermometer (Genius FirstTemp, M 3000A, Sherwood medical, Sussex, UK).
Each individual underwent a dialysis session in week 1 with the blood flow set at 300 ml/min. A second session at 200 ml/min was performed in the second week. The sequence of flow levels was randomly assigned for each of the participants. Before and after a dialysis session, blood samples were taken to determine levels of urea, kreatinine and potassium to evaluate the efficacy of dialysis. Both measurement sessions were started on identical points of 2 similar days of consecutive weeks.
Hemodialysis was performed using Hospal Integra® dialysis monitors equipped with Polysulfone dialysis membranes (F8HPS; Fresenius®). The dialysate contained potassium (2.0 mmol/l), calcium (1.5 mmol/l), magnesium (0.5 mmol/l), bicarbonate (32 mmol/l), acetate (3.0 mmol/l), glucose (1 g/l) and sodium (140 mmol/l). The temperature of the dialysate was 36°C. Heparine was provided in standard amounts (5000 IU). Patients were ultrafiltered until they had clinically attained their estimated dry weight (-2.2 ± 0.4 l (200 ml/min) and -2.5 ± 0.4 l (300 ml/min), ns).
Access flow (ml/min) was measured in duplicate within 2 weeks prior to the study weeks using a dilution technique with a Transonic flow meter (HD01, Transonic Systems Inc, New York, USA) (9).

STATISTICAL ANALYSIS

Statistical analyses were performed with SPSS (15.0). Blood urea, kreatinine and potassium concentrations before and after dialysis were compared with the Wilcoxon signed rank test. A two-way ANOVA for repeated measurements was performed for intradialytic measurements with two different dialysis blood flows. Data were expressed as mean ± sem. A $p<0.05$ was considered significant.

RESULTS

Study group

Fifteen patients were eligible for study, but three refused to undergo all measurements for personal reasons whereas two others were unwilling to undergo measurements during their second dialysis session. Eventually, ten patients completed the protocol of both dialysis sessions (5 males, 5 females, mean age 68±5 years). All were on chronic hemodialysis (>3 mo) and they all harboured autogenous AVF's (brachiocephalic n=8, transposed basilic vein n=2). Four patients were diabetic, and three other hypertensive patients used β-blocking agents or calcium entry blockers. The study population's comorbidity is depicted in the table.
Mean access flow was 1125±174 ml/min (range 240-2325 ml/min). They effectively dialysed at the 300 and 200 ml/min level as concentrations of urea, kreatinine and potassium changed in a similar fashion. There were no significant differences in ultrafiltration rates during both dialysis sessions (data not shown).

Effect of dialysis on vital and other parameters

Intensity of ischemic symptoms did not change during the 3-4 hour 300 or 200 ml/min sessions. SBP and MAP significantly decreased over time ($p=0.003$ and $p=0.007$, respectively), at both levels of blood flow in a similar fashion. Alterations in MAP are shown in the upper panel of figure 2. Immediately after dialysis, a tendency towards recovery was observed. A significant decrease in HR ($p<0.01$) was also demonstrated during the first hour of dialysis (lower panel figure 2). Alterations in HR were again independent of artificial kidney's blood flow.
Prior to dialysis, P_{dig} of the AVF hand was approximately 55 mmHg lower compared to the contralateral hand (137±10 vs 82±8 mm Hg, $p<0.01$). P_{dig} on the AVF side decreased significantly at both flow levels ($p<0.01$), and artificial kidney's flow level did not influence these differences. The responses by either hand were statistically near identical ($p=0.97$). DBI demonstrated a similar response (figure 3). An almost significant drop ($p=0.065$) in

Patient characteristics (n=10)	
Male / Female (n)	5 / 5
Age (mean) (years)	68 ± 5
Diabetes mellitus (n)	4
Hypertension (n)	3
Peripheral arterial occlusive disease (n)	4
TIA/CVA* (n)	2
Cardial (n)	3

Table ***Characteristics of the study population*** ** TIA: Transient Ischemic Attack / CVA: Cerebro Vascular Accident*

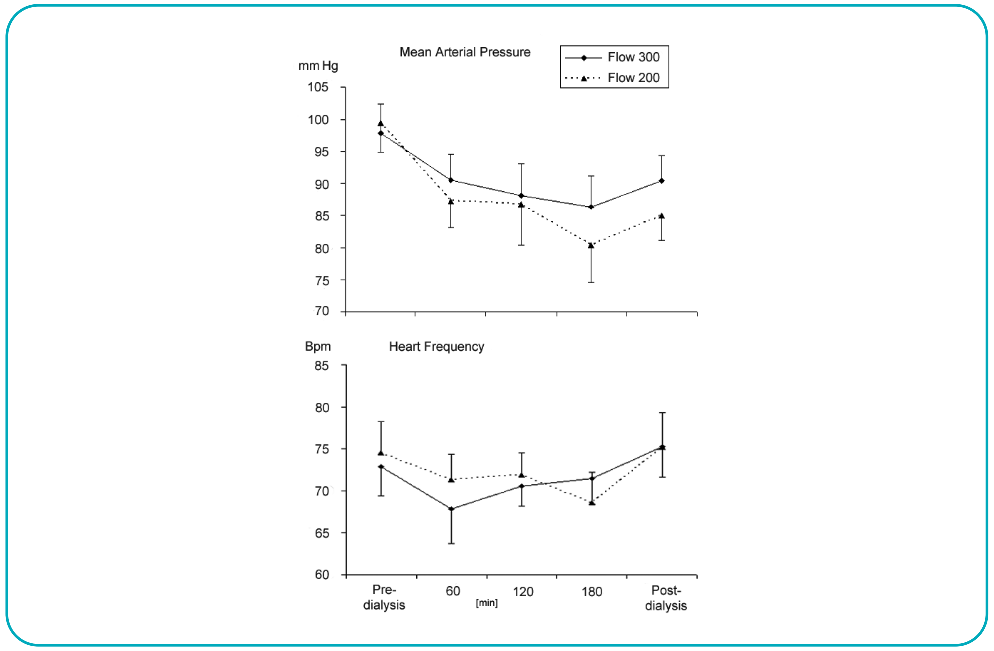

Figure 2 Mean arterial pressure and heart rate drop immediately after onset of dialysis (p=0.007). A difference between groups was not observed

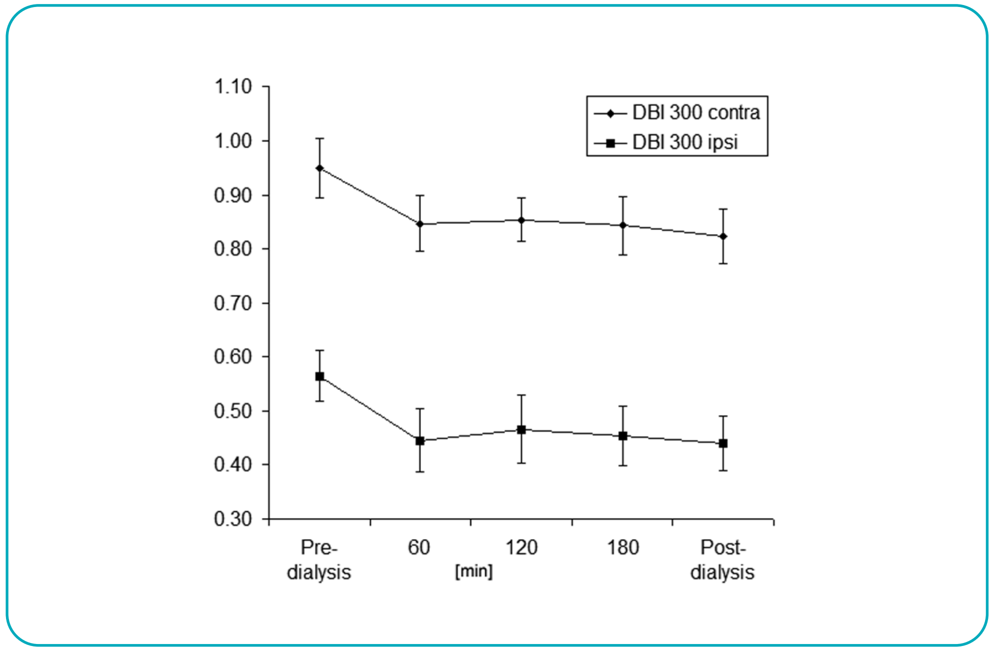

Figure 3 Alterations in Digital Brachial Index (DBI) of the AVF hand (ipsilateral) and the other (contralateral) hand during the 300 ml/min dialysis sessions

DBI on both hands was observed during the first hour of dialysis. Saturations remained stable and were also independent of blood flow.

T_{dig} of the AVF's hand was on average 1.5 °C lower compared to the contralateral hand (27.2±1.0 vs 28.8±1.0 °C, $p<0.05$). During dialysis, temperatures at both levels of blood flow remained unaltered ($p=0.354$). There were also no changes in body temperature during the dialysis sessions (36.4±0.3 to 36.6±0.3 °C).

DISCUSSION

Previous studies have found that patients with hemodialysis access-induced distal ischemia (HAIDI) demonstrate low P_{dig} and T_{dig} during rest (2,10). Moreover, during a hemodialysis session some patients incidentally report intensification of symptoms traditionally associated with ischemia. Aim of the present investigation was to monitor the effects of two different regimens of hemodialysis blood flow on ischemic symptoms, digital perfusion and T_{dig}. We hypothesized that hemodialysis-induced alterations in P_{dig} were depended on artificial kidney blood flow. The present results indicate that, prior to dialysis, P_{dig} and T_{dig} of an AVF hand were on average 55 mm Hg and 1.5 °C lower compared to the other hand, respectively. The onset of dialysis immediately induced an extra 20 mm Hg pressure drop in the AVF hand. However, a drop of similar magnitude was also observed in the other hand. Alterations in P_{dig} were independent of blood flow but mirrored changes in SBP/MAP. If one accepts the premise that low P_{dig} reflects HAIDI, conservative treatment of HAIDI may also include measures aimed at attenuating declining values of SBP.

Patient selection of the present study is arbitrary. It was assumed that any hemodialysis associated hypotensive effects on hand perfusion were large in individuals reporting intensification of symptoms of HAIDI during the course of a dialysis session. Recent studies have focused on quantifying HAIDI using a questionnaire. Patients reporting mild to moderate HAIDI had scores ranging from 35–50 points on a 0-500 scale (2). In contrast, values obtained in another study reporting on severe HAIDI patients requiring corrective surgery were 153±33. Successful surgery reversed these high values towards normal (42±15) (8). The present study population demonstrated high normal values (between 50-60), and these numbers were stable during the 3-4 hour dialysis sessions. Individuals with more intense HAIDI (as reflected by higher scores e.g. >100) may have responded differently to the measurement protocol compared to the present population. SBP and MAP demonstrated a characteristic pattern during the course of a dialysis session. Moreover, a lowered HR was observed during the first hour of dialysis. This disturbed homeostatic compensatory mechanism in hemodialysis patients has been observed previously and may be related to reduced arterial and venous reactivity associated with release of nitric oxide and cytokines, dialysis membrane bioincompatibility, characteristics of the dialysate (acetate) and insufficiently increased levels of vasoconstrictors such as vasopressin (11,12). Depending on the temperature of dialysis fluids, core temperature may increase during dialysis leading to dilated cutaneous arteries and veins and even more progressive hypovolemia (13). Conversely, when dialysis fluid temperature was lowered to 35-36 °C, an improved response in vascular reactivity and more stability of blood pressures were found (14). Body temperature of the present population remained stable between 36.4 and 36.6 °C during the hemodialysis using a 36 °C dialysate. A further lowering of the dialysate temperature may diminish the drop in SBP and associated P_{dig} and may attenuate symptoms of HAIDI during the dialysis. However, lowering temperatures of the dialysate should be balanced against the potential induction of uncomfortable feelings.

Most investigators consider the digital brachial index as a measure of hand perfusion (DBI, ratio of P_{dig} to SBP, normal 0.8-1.0). However, the reliability of a cut-off point for intense hand ischemia is controversial. A DBI <0.6 during routine access surgery is associated with a risk of postoperative HAIDI (10). Other studies reporting on severe HAIDI found a DBI <0.45 although positive predictive values were limited (15,16). Mean DBI in the present study population was 0.53±0.03, and a drop to 0.44±0.05 was found at various time points during the dialysis. Interestingly, patients did not report an intensification of the ischemic symptoms throughout the course of the dialysis session as scores using the questionnaire remained stable. These low DBI values in the absence of severe ischemic symptoms possibly illustrate the limited value of absolute cut-off points of DBI representing various grades of hand ischemia.

The role of digital pulse oximetry in monitoring hemodialysis access induced digital ischemia is questioned. Oxygen saturation levels <80% were found in patients with severe HAIDI (17,18). In contrast, levels obtained from the AVF hand in another study were not different from the contralateral hand in patients with moderate HAIDI (92±1 vs 93±2 %)(2). Significantly reduced flows to the hand also did not influence pulse oximetry readings (19). Several studies reported on continuous measurement of oxygen saturation during dialysis. Values <90% were found in half of the patients in a dialysis population (7). Another study reported an asymptomatic 1.9% drop of oxygen saturation after the onset of dialysis, most prominently in the first hour (6). An asymptomatic decrease in saturation may reflect the combined result of hypotension and hypoventilation due to CO_2 loss by the dialyzer. As none of our 10 patients showed a decline in oxygen saturation throughout all dialysis sessions in the presence of substantially decreased finger pressures, digital pulse oximetry is probably not helpful in monitoring hemodialysis induced digital ischemia.

An important finding of the present study is the fact that alterations in P_{dig} occurred independently from the artificial kidney's blood flow during dialysis. Levels of blood flow are generally maintained between 250 and 300 ml/min in our dialysis center. These blood flows are easily generated by most AVF's as the majority has flows well above 600 ml/min (1125±174 ml/min). If gradually diminishing access flows approximate blood flow to the artificial kidney, negative pressures may create increased pressure gradients relative to the hand. A normal arterial system of the arm may compensate for this loss in distal perfusion pressure but diabetics with diseased and stiffened arteries may not. A subjective increase in ischemic symptoms may therefore reflect declining access flows, particularly in patients with diabetes or peripheral arterial disease.

Conclusion

P_{dig} and T_{dig} of an AVF hand are lower compared to the other hand. Onset of dialysis immediately induces an extra pressure drop in the AVF hand, but decreased values of similar magnitude are also observed in the other hand. Alterations in P_{dig} appear independent of hemodialysis blood flow (range 200-300 ml/min) but mirror changes in SBP. Attenuating lowered SBP during dialysis may reverse digital ischemia associated with hemodialysis treatment.

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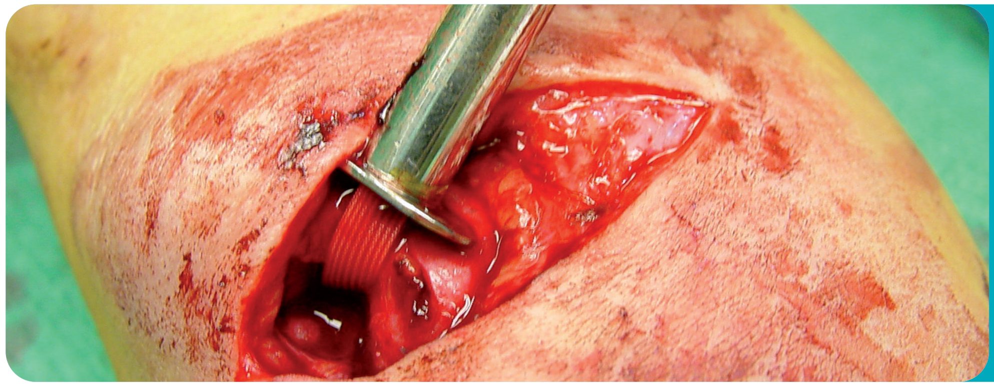

CHAPTER 4

Surgical banding for refractory Hemodialysis Access-Induced Distal Ischemia

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ABSTRACT

Hemodialysis patients may develop distal ischemia in an extremity harboring a functioning arteriovenous fistula (AVF). Surgery is indicated if conservative treatment including catheter-based therapies fails. The role of surgical banding for refractory hemodialysis access-induced distal ischemia (HAIDI) is systematically reviewed (n=39 articles). If banding is executed without an intraoperative monitoring tool ("blind"), or guided by finger pressures only, clinical success and access patency rates are low (<50%). In contrast, banding is clinically successful when access flow is monitored during the operative procedure, with excellent long-term patency of banded AVF's (97%, 17 ± 3 months). Banding is the method of choice in HAIDI patients with a normal or high access flow (>1.2 l/min) provided that flow and distal perfusion are closely monitored intraoperatively.

Figure 1 *Hemodialysis access-induced distal ischemia (HAIDI) with digital necrosis.*

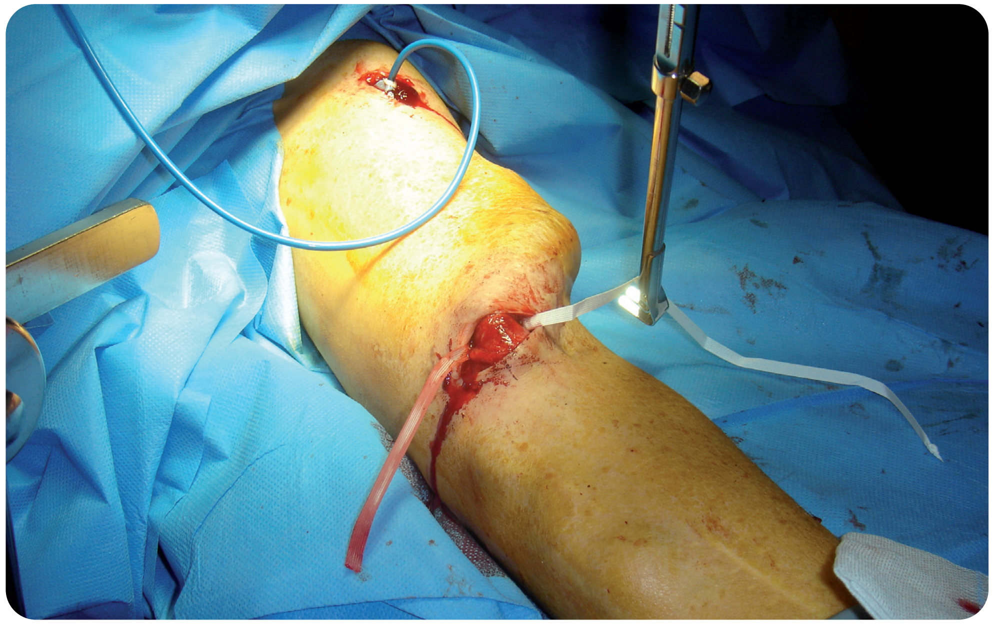

Figure 2 *Intraoperative view of banding of an AVF guided by monitoring of access flow (blue probe) and digital plethysmography (not shown). A 5 mm wide band is wrapped around venous outflow followed by fixation using a metal clip and prolene stitches. Alterations in access flow and finger pressures determine grade of banding (59, 60).*

INTRODUCTION

Most arteriovenous fistulas (AVF's) created for hemodialysis (HD) treatment do not compromise distal limb perfusion. However, a small group of patients develops ischemia of the distal tissues shortly after routine access construction, or later on (1). Severe prolonged intense ischemia may result in loss of function and tissue (figure 1) necessitating the amputation of fingers, hand or even forearm (2, 3). The cause of distal ischemia in the presence of an AVF is under debate. Some investigators consider "steal" important in hemodialysis access-induced distal ischemia (HAIDI) (4, 5). However, ischemic events are due to the loss of perfusion pressure in the presence of a low resistance AVF (6). In other words, blood pressure (BP) distal to the AVF is too low to secure an adequate level of distal tissue perfusion.

As ischemic symptoms in mild or moderate HAIDI frequently diminish over time, a first line of treatment should always be conservative. Initial management includes the modification of antihypertensive medication whereas vasospasmolytic medication (nifedipine) appeared helpful in selected cases (7). Statins, antiplatelet and rheological agents may prove valuable in HAIDI but have not been systematically studied. When ischemic symptoms intensify during HD, flow reduction through the artificial kidney or warm hand dressings may promote acral perfusion. If these conservative strategies fail, catheter-based techniques may identify stenotic lesions in the arterial inflow tract (4). Hemodynamically active atherosclerotic plaques are treated by angioplasty and/or stenting. However, more invasive treatment is indicated if ischemic symptoms are not abolished by successful endovascular treatment.

A small portion of patients with refractory HAIDI require vascular surgery. Distal revascularization and interval ligation (DRIL) (8), AVF outflow banding (9) or proximalization of inflow (10) are currently promoted for refractory HAIDI. Banding was introduced in the 1970s (9, 11), discussed in the 1980s (12), and was viewed with scepticism in the 1990s following dismal post-operative access patency rates (4, 13, 14). Theoretically, banding increases the access' outflow resistance by narrowing the AVF's efferent vein adjacent to the anastomosis. Future vein dilation is prevented by the application of a non-resorbable restrictive band (figure 2) (15). The technique is simple and physiologically sound but its efficacy is questioned. The purpose of this overview is to investigate the short- and long-term efficacy of banding for refractory HAIDI.

METHODOLOGY AND DEFINITIONS

PUBMED and Google were searched using the terms arteriovenous access, fistula, hemodialysis, banding, access, graft, steal, DASS (dialysis associated steal syndrome), digital, hand, and ischemia in combination with the Boolean operators AND and OR. Reference lists of identified publications published between 1966 and June 2008 were checked for additional English, German, French, Italian and Spanish medical literature. Studies including cases were eligible for analysis if clinical success was reported (100% success, total recovery from ischemic symptoms; 50% success, partial recovery; or failure) as well as the use of intraoperative monitoring tool(s), and AVF occlusion rate (<3 months). "Blind" banding is defined as the application of a constrictive band without the use of an intraoperative tool monitoring effects on access flow and/or distal perfusion. Mean access patency of successfully banded AVF's was calculated as total FU months/number observed patients.

RESULTS

Thirty-nine articles fulfilled the inclusion criteria (4, 5, 9, 11, 12, 14-47). Table I depicts the clinical results of blind banding in the upper panel. Dismal results were observed as only 6/20 patients reported relief from ischemia. Moreover, 40% (8/20) of the blindly banded AVF's occluded (table 1). In addition, banding guided solely by increased systolic finger pressures as measured by intraoperative digital plethysmography also resulted in unacceptable access occlusion rates (51%, 18/35 occlusions).

Table I provides data on banding guided by other monitoring tools in the lower panel. In contrast, flow measurements (access or arm), return of palpability of radial pulses, intraoperatively attenuated symptomatology reported by a locally anesthetized patient, pulse volume recording (PVR), pulse oximetry, Doppler measurements and angiography all provided information that contributed to a clinically successful banding procedure as 89% (152/170) reported total relief from digital ischemia. Long-term patency of successfully banded AVF's is excellent being 97% (148/152, mean FU 17 ± 3 months).

DISCUSSION

The aim of this overview was to investigate the short and long-term efficacy of a surgical treatment termed banding for refractory HAIDI. Many consider banding a somewhat controversial modality for HD access induced ischemia as high AVF occlusion rates were observed immediately following banding (4, 14, 26). If banding is executed without the guidance of an intraoperative monitoring tool ("blind") or solely aided by measurements of increased systolic finger pressures, clinical success and access patency rates are in- deed unacceptable (40-60%). These suboptimal access patency rates obtained with finger pressure control can be explained by the fact that minimal access flows just above the thrombosis threshold level are not guaranteed. It is likely that some accesses may have been "overbanded" as (too) high finger pressures were strived for. Another disadvantage of plethysmography is the inherent non-invasive determination of finger pressures at a "systolic" level. These values only contribute about 30% to "mean" arterial pressures, the latter considered more crucial for tissue ischemia.

Author	Yr	Pt	100% success	50%	0%	Intraoperative control tool	Occlusion < 3 mo (n)	FU (mean, mo)
Tellis (11)	1979	1	0	0	1	blind	1	-
Wytrzes (16)	1987	2	0	2	0	blind	0	4
Dally (17)	1987	1	0	1	0	blind	0	8
Wahl (18)	1997	2	1	0	1	blind	0	-
Sessa (19)	2000	1	0	0	1	blind	1	-
Valentine (20)	2002	1	0	0	1	blind	1	-
Mwipatayi (21)	2006	1	0	0	1	blind	1	-
Nazzal (22)	1990	3	3	0	0	blind	0	-
Chia (23)	1999	1	0	0	1	blind	1	-
Seror (24)	2006	1	0	0	1	blind	0	-
Haimov (25)	1975	2	2	0	0	blind	0	12
Haimov (26)	1996	4	0	1	3	blind	3	-
Odland (14)	1991	16	10	6	0	PPG	6	6
Stierli (27)	1998	6	5	0	1	PPG	3	2
DeCaprio (4)	1997	11	10	0	1	PPG	9	-
Mattson (28)	1987	2	2	0	0	PPG	0	-
Subtotal I		**55**	**33**	**10**	**12**		**26**	
Zanow (29)	2006	78	67	11	1	Flow	3	25
DePalma (9)	1973	1	1	0	0	Flow	0	-
Kwun (30)	1979	2	2	0	0	Flow	0	-
Thermann (31)	2007	15	10	0	5	Flow	1	27
Meyer (32)	2002	7	7	0	0	Duplex	0	36
Jain (15)	1992	3	3	0	0	Duplex	0	-
Aschwanden (33)	2003	2	2	0	0	Duplex	0	-
Shemesh (34)	1999	3	3	0	0	Duplex	0	28
Schild (35)	2001	7	7	0	0	Pulsations	0	12
Stary (36)	2002	4	4	0	0	Pulsations	0	1
Montoya (37)	1993	1	1	0	0	Pulsations	0	-
West (38)	1991	2	2	0	0	Pulsations/PGG	0	2
Khalil (39)	1988	6	6	0	0	Pulsations/symp	0	10
Papalois (40)	2001	1	1	0	0	Pulsations/symp	0	4
Ozisik (41)	2003	6	6	0	0	Puls/thrill/Duplex	0	6
Stanicia (42)	1997	1	1	0	0	Symptomatology	0	12
Goel (43)	2006	16	15	1	0	Sympt/Angio	0	3
Halevy (44)	1991	5	5	0	0	Pulse oximetry	0	-
Pomper (45)	2000	2	2	0	0	Pulse oximetry	0	17
Rivers (5)	1992	5	4	1	0	PVR	0	4
Ebeid (12)	1981	1	1	0	0	Doppler rad art	0	-
Porcellini (46)	1997	1	1	0	0	Doppler rad art	0	35
White (47)	1999	1	1	0	0	Doppler rad art	0	9
Subtotal II		**170**	**152**	**13**	**6**		**4**	
Mean								**17**
Total		**225**	**185**	**23**	**18**		**30**	

Table 1 ***Clinical success of banding and intraoperative monitoring***

Clinical success is defined as total abolishment of ischemic symptomatology, 50% as partial, and 0% as total failure. Blind, without monitoring tool. PPG, photoplethysmography. Flow, access flow by electromagnetic/ultrasound. Duplex, combined Doppler/ECHO. Pulsations, as determined by palpating radial artery. Symptomatology, as reported by patients. Angio, angiographic findings. Pulse Oximetry, oxygen saturation. PVR, pulse volume recordings. Doppler, signal analysis of radial artery. If surgical banding is executed without any intraoperative monitoring tool ('blind') or solely guided by increased finger pressures (n=55 patients), both clinical success (60%, 33/55) and access patency rates (53%, 29/55) are unacceptably low. In contrast, banding is clinically successful (89%, 152/170) when guided by intraoperative measurements of access flow combined with return of pulsations or finger pressures using photoplethysmography (n=170 patients). Long term patency (mean FU 17 ± 3 months, mo) of successfully banded AVF's is excellent (97%, 148/152).

Transcutaneous oxygen measurements or laser Doppler analysis may reflect tissue perfusion more accurately than systolic finger pressures but have not been performed in HAIDI (48, 49). This overview clearly demonstrates that banding is clinically very successful if both access flow and distal arterial pressure are monitored simultaneously during the operative procedure. Ischemia is totally (89% of patients) or partially (another 8%) abolished, while successfully banded AVF's usually (97%) remain patent during the 17 month follow-up period.
Each HAIDI patient deserves a tailored treatment plan designed by a multidisciplinary team consisting of a nephrologist, an interventional radiologist and a vascular surgeon. If ischemic symptoms occur immediately (hours) after a routine access construction, emergent (within hours) surgical correction is mandatory (50). The access anastomosis is narrowed or ligated. In contrast, if HAIDI develops over months to years after access construction, hand ischemia is due to progressive loss of perfusion pressure following AVF maturation or ongoing atherosclerosis of the arm arterial vasculature. Initial treatment is conservative aimed at increasing BP and stimulating hand perfusion using a combination of vasospasmolytic medication (eg nifedipine), antiplatelets, rheological agents (eg pentoxyfylline), or statins. Cold hands may be warm packed while artificial kidney flow is reduced. If conservative strategies fail, AVF inflow and outflow must be visualized using angiography (4). If endovascular treatment of stenotic lesions is ineffective in abolishing HAIDI, invasive surgery may offer relief. About 4-7% of patients belonging to a mixed dialysis population eventually require surgical intervention. However, incidences of surgery may be up to 17% (51) and even 33% (52), depending on the index of suspicion and operative tactics. Prior to embarking upon invasive therapy, it must be established whether salvage of the causative access is mandatory. Questions on its functioning and condition of the contralateral arm need answering. Alternative dialysis treatments including catheter access or peritoneal dialysis need exploring. If these dialysis facilities are rejected, HAIDI should be treated with a corrective technique that does not endanger the access' patency and is ideally "minimally invasive". It must also be realized that patients with HAIDI have a limited life expectancy as mortality rates up to 35% in the first 6 post-operative months following corrective vascular surgery have been reported (53).
Apart from banding, several other techniques are promoted including distal revascularization interval ligation (DRIL) (51) and proximalization of arterial inflow (PAI) (10). DRIL assumes that HAIDI is due to insufficient capacity of arterial collaterals securing adequate distal limb perfusion (6). A short autologous vein bypass is constructed between the artery proximal to the AVF and the arterial vasculature distal to the AVF. The artery just distal to the AVF is subsequently ligated; therefore, preventing "attraction" of blood from peripheral limb portions (54). Some issues regarding this technique are incompletely understood. Both steps of the procedure are not always necessary since ligating without bypassing normalized distal perfusion in one patient (55). On the other

hand, patients with distal atherosclerosis of the arms (6) or legs (56) successfully received a bypass and did not require ligation. A promising novel technique is termed PAI. The arterialized vein of a brachial-cephalic access is disconnected and subsequently reconnected with a 4-5 mm prosthetic bypass originating from a more proximal portion of the inflow vasculature. This technique saves the access while HAIDI is effectively abolished (10).
What is the place of banding in the surgical spectrum for HAIDI? Type of operative procedure must be determined by access flow. Patients with normal to low flow (between 1200 and 300 ml/min) are preferentially treated by DRIL or PAI. Long-term bypass patency in DRIL is favorable, and ischemia is effectively abolished (51). As DRIL theoretically increases access resistance, flow may subsequently be reduced but occlusions are rare. Disadvantages include complexity and risk of disturbed wound healing, whereas the efficacy of DRIL for cardiac overload is largely unknown. PAI is a valuable alternative in normal and low flow HAIDI as it maintains access flow (10). Patients with normal to high access flow (>1200 ml/min) are preferentially treated by banding. The likelihood of successful banding is optimal if the operative procedure is directed by (at least) two monitoring tools, one for serial measurements of access flow (to prevent access thrombosis) whereas the second tool (photoplethysmography?) monitors improvement of distal perfusion. Advantages of banding are simplicity, performance under local anesthesia and efficacy of reducing associated cardiac overload, a possible cause for increased mortality rates in HD patients (9). A theoretical disadvantage of banding is the onset of turbulence and subsequent intimal hyperplasia causing further narrowing (12). However, diminished intimal hyperplasia was found at the level of bands in a controlled animal model (57). This theoretical disadvantage appears clinically irrelevant as this overview demonstrates excellent access patency rates of successfully banded AVF's.
This overview suffers from various types of bias. Publication bias may have influenced results as surgeons could have been reluctant to share negative experiences with banding. Selection bias is minimized as inclusion criteria for analysis were strict. It was decided only to evaluate studies reporting on clinical success as well as intraoperatively used monitoring tool(s) and AVF occlusion rates (<3 months). Clinical success was defined in terms of total recovery from ischemic symptoms, partial recovery, or failure. However, studies extracted from the literature frequently described ischemic symptoms in subjective terms including persistent pain (21), intolerable pain (41), severe pain (40), or just pain (44). Effects of banding on digital ischemia are usually reported in similar terminology. A non-standardized way of reporting ischemic symptoms complicates proper treatment evaluation. A recent study suggests scoring ischemia on a 0-500 point scale. Both frequency and intensity of five cardinal symptoms (coldness, pain, cramps, diminished sensibility and strength) contribute 0-100 points each to this ischemic score (58). Quantification of hand ischemia may facilitate the evaluation of the efficacy of treatment strategies and may allow for comparison of study results.

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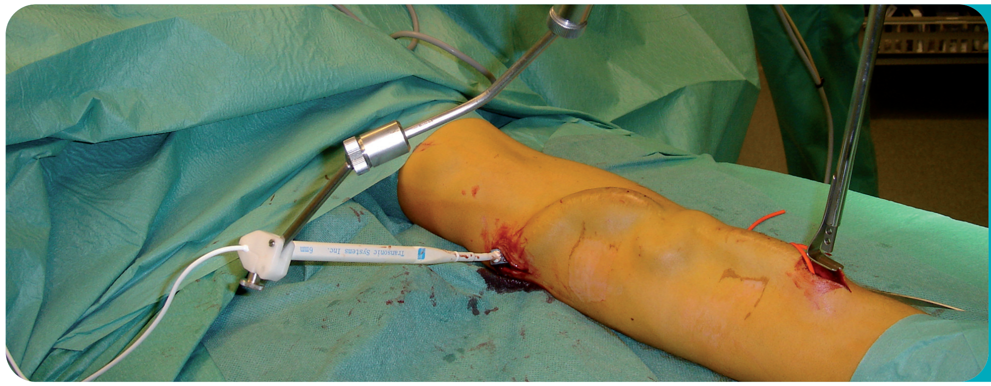
CHAPTER 5



Access flow, venous saturation and digital pressures in hemodialysis

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ABSTRACT

Introduction

A hemodialysis arteriovenous fistula (AVF) requires surgical modification in patients with cardiac overload (CO) or dialysis access-associated steal syndrome (DASS). Creation of an artificial stenosis ('banding') within the AVF may be used, but this technique lacks the guidance of objective parameters. The aim of this pilot study was to identify indicators that reflect AVF flow in dialysis patients with either access related CO or DASS requiring corrective surgery.

Materials and methods

Patients underwent serial measurements of subclavian venous saturation (Sat_{ven}), access flow ($Flow_{us}$) and index digital pressures (P_{dig}) during a corrective banding procedure.

Results

Data were obtained in 14 individuals (9 men, mean age: 53±6 years) during 16 studies (CO n=8, DASS n=8). Before surgery, correlations between preoperative flow, Sat_{ven} and P_{dig} were not significant. Stepwise banding of the AVF altered Sat_{ven} in both groups from a mean of 91±1% (open AVF) to 84±2% (closed AVF, $p<0.001$). CO-patients demonstrated a larger drop (-13%) compared to DASS-patients (-4%). Values of P_{dig} increased from 68±9 to 90±9 mm Hg ($p<0.001$), and both groups demonstrated a similar +23 mm Hg increase. In concert, the digital brachial index also significantly improved in al patients from 0.60±0.09% to 0.74±0.10%. Linearity was present between alterations in $Flow_{us}$ and Sat_{ven} in all patients but mostly in CO-patients ($r^2=0.96$).

Conclusions

Stepwise banding of hemodialysis fistulas leads to dose-dependent decreases in flow and ipsilateral subclavian venous saturation combined with augmented digital pressures in patients with cardiac overload and dialysis associated steal syndrome. Intra-operative measurements of venous saturation and digital pressures may have the potential of guiding surgical correction in these patients.

INTRODUCTION

A hemodialysis arteriovenous fistula (AVF) seldomly causes severe regional or systemic hemodynamic disturbances. Incidently, augmented access flows may lead to chronic cardiac overload (CO) (1,2). Some AVF's may steal blood from peripheral portions of extremities leading to hand ischemia (dialysis access-associated steal syndrome (DASS)) (3,4). Eventually such AVF's may have to be disconnected requiring temporary alternative methods of dialysis and additional surgical procedures. Surgery aimed at modifying a malfunctioning AVF (e.g. banding) is frequently avoided or postponed because parameters that may guide such procedures appear to lack accuracy (5-10).
Under physiological conditions, arterial blood is associated with high concentrations of saturated hemoglobin in contrast to venous blood. An AVF allows arterial blood to flow into the venous vasculature. Therefore, highly saturated blood will mix downstream with venous blood of low saturation ('shunting'). As a consequence, relatively high values of saturation may be measured in upper arm or subclavian veins in the presence of an AVF. It may be hypothesized that levels of venous saturation (Satven) are thus related to AVF flow. The association between access flow and venous saturation has not been studied in hemodialysis patients.
DASS is characterized by a clinical syndrome including pain, coldness and hand ischemia. A range of parameters possibly reflecting this condition has been studied, but only low finger pressures (P_{dig}) and lower index digital temperatures were associated with DASS (11). A digital arm index below 0.6 is associated with severe steal (12,13). One may assume that alterations in digital pressures are related to changes in access flow (9).
The general goal of this pilot study was to identify objective parameters that reflect AVF flow in dialysis patients with access related CO or DASS. The following hypotheses were formulated. 1. Satven in the ipsilateral subclavian vein is related to access flow 2. Manipulating access flow will lead to alterations in P_{dig}.

MATERIALS AND METHODS

Study population

This pilot study was performed between January 2003 and April 2006 in the Maxima Medical Center, Veldhoven, The Netherlands, a community hospital of 865 beds in the southeastern part of the Netherlands serving approximately 350.000 inhabitants. The dialysis center accomodates 90 hemodialysis patients. A total of 273 AV-access cases were performed in this 3 year time period.
Patients undergo access surveillance with regular measurements of blood flow and venous pressures as proposed by DOQI (14). Access flow is measured in duplicate every two months using standard two-needle dilution techniques (HD01, Transonic Systems Inc, New York, USA) (15). Patients were eligible for study if they were on chronic hemodialysis (> 3 months). All were scheduled to undergo corrective surgery because of CO or DASS, as advised by their cardiologist and/or nefrologist. They could participate in the study if they met at least one of the following criteria:

1. a consistently (≥ 3 measurements) high output dialysis AVF (≥ 2.0 l/min), with or without cardiac symptomatology such as palpitations and cardiac failure.
2. debilitating ischemia of the dialysis hand.

They were informed on the nature of the study and consented to its specifics. Patients were not studied if they refused, or if a language barrier was present.

Study protocol

Surgery was performed under general anesthesia using etomidate and sufentanil for induction. After intubation facilitated by mivacurium, anesthesia was maintained with sevoflurane. Following intubation a triple-lumen central venous line (CVL) (Central Venous Oximetry Catheter with AMC Thromboshield, Edwards Lifesciences, Irvine, USA) was introduced in the ipsilateral subclavian vein using a percutaneous puncturing technique. Line positioning was such that only the most distal port was located in the subclavian vein itself allowing continuous measurements of Sat_{ven} reflecting true arm values without jugular contributions. Correct CVL positioning was checked postoperatively using a chest radiograph.
A photoplethysmographic sensor was placed on volar portions of the top of the ipsilateral index finger. An inflatable cuff was wrapped around the finger's proximal part allowing repetitive P_{dig} measurements (VasoGuard Nicolet, 8 Mhz, Scimed Ltd, Bristol, UK). Following arm and axillar desinfection the arteriovenous anastomosis was dissected including its arterial and venous portions. At least 10 cm downstream towards the axilla, an additional 1.5 cm incision allowed dissection of a second portion of upper arm cephalic or basilic vein. The space between vein and a 4-8 mm probe was filled with acoustic gel. This site was then used for online access flow measurements using an ultrasonic transit time technique (HT 313, Transonic Systems Inc, New York, USA). Measurements were only performed if a stable signal was achieved with >90% accuracy as advised by Transonic.
Following a 5 min equilibration period, a 5 mm wide flat woven polyester band (Mersilene, Johnson & Johnson, Hamburg, Germany) was loosely wrapped around the venous portion within 2 cm from the arteriovenous anastomosis. Both ends of the band were positioned into a specially designed metal pulling mechanism (figure 1). By clockwise turning a wheel attached on top of this puller, the band progressively narrowed the venous portion of the arteriovenous anastomosis ('banding'). A metal rod fixed to the operation table both holding the puller and the ultrasonic flow probe guaranteed a

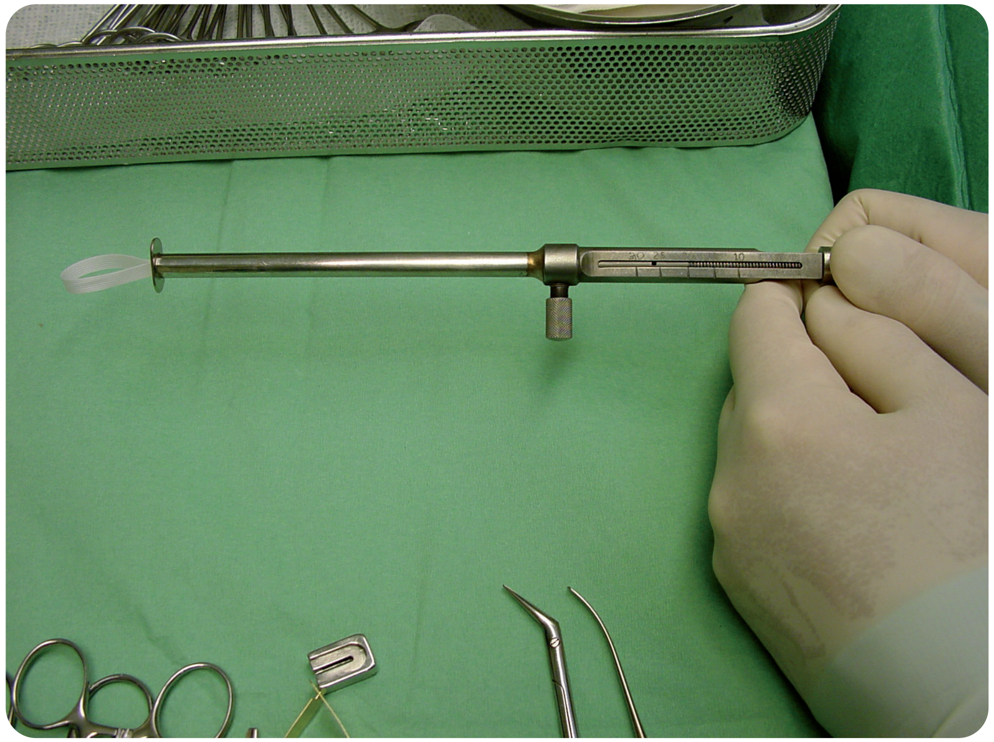

Figure 1 Constriction of the arteriovenous fistula with a 5-mm flat woven polyester band occurs by the clockwise turning of a wheel mounted on top of a specially designed metal puller. This experimental design allows a detailed study of the correlation between arteriovenous fistula flow, venous saturation, and digital pressures.

stable measuring system in the absence of movement artefacts (figure 2). All banding procedures were performed by one surgeon (MS). Monitoring of vital signs including blood pressure, heart frequency, ventilation and contralateral digital saturation was left to the discretion of one anesthesiologist (ML).

Definitions and Measurement protocol

Access flow as measured preoperatively by a dilution technique in the dialysis ward is expressed in l/min and is termed $Flow_{preop}$. The upper limit of $Flow_{preop}$ is 4 l/min as determined by the HD01 Transonic device. Intraoperative access flow measured by a flow probe using ultrasonic transit time methods is termed $Flow_{us}$. Digital pressures (P_{dig}) are expressed in mm Hg. A digital brachial index (DBI) was calculated as the ratio of P_{dig} to intraoperative systolic blood pressure.
To study the effects of stepwise narrowing of the band, a maximal stable value of $Flow_{us}$ was determined at the beginning of the operation and was arbitrarily set at 100%.

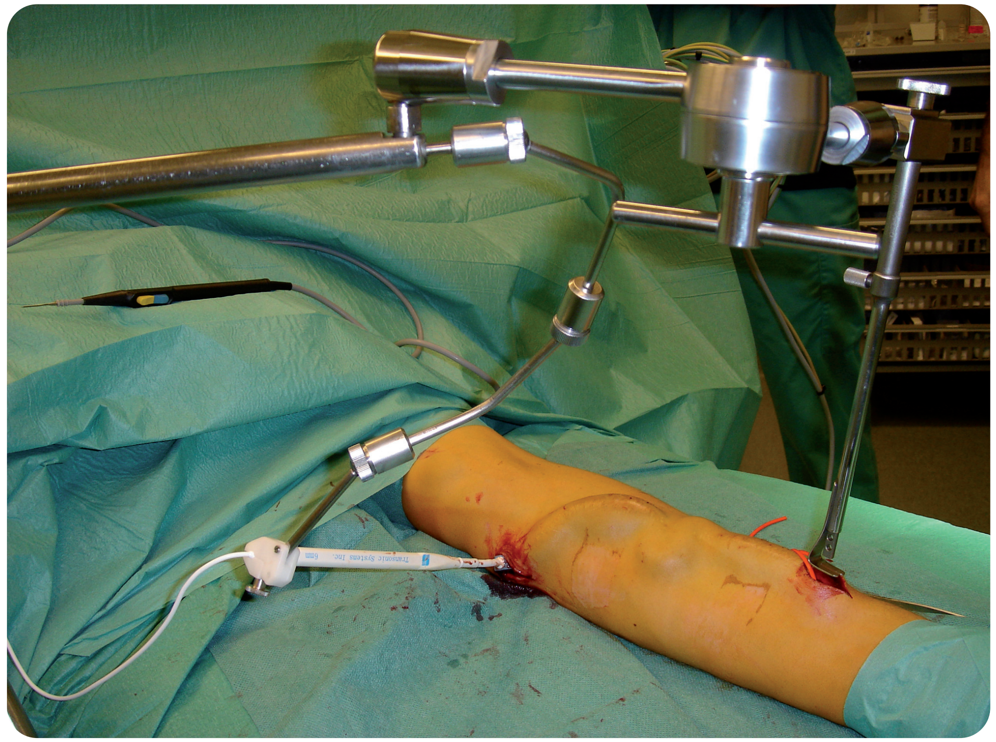

Figure 2 Intraoperative view of a banding procedure. Flow is measured at the level of the upper arm by an ultrasound probe. Narrowing of the arteriovenous fistula using a puller is performed at the level of the anastomosis. The probe and the puller are both held by a metal arm fixed to the operating table, allowing absence of movement artefacts in an anesthetized patient.

Constriction of the band was performed in 25% decrements in $Flow_{us}$ as depicted by the online flow meter. Associated alterations in Sat_{ven} and P_{dig} at these time points were tabulated.

STATISTICAL ANALYSIS

The data of Sat_{ven} as a function of $Flow_{preop}$ was fitted using a least squares fitting algorithm and Pearson's correlation coefficient was calculated using SPSS statistical package (version 12.0.1). A Student t-test was used to determine whether a trend was significant. This method was also performed to determine the significance of group differences in Sat_{ven} following stepwise banding. Paired t-test was used to evaluate differences between open and closed AVF's in Sat_{ven}, P_{dig} and DBI. Results were expressed as mean ± s.e.m. A $p<0.05$ was considered significant.

RESULTS

Fifteen patients were eligible for study, but one patient refused surgery for personal reasons. Two patients were studied twice (recurrent high output after 27 months (n=1); malpositioning of the central venous line (n=1). Data thus reflect 16 studies in 14 different individuals (CO n=8, DASS n=8). Characteristics of the study population are depicted in the table. Two patients with DASS suffered from diabetes mellitus. $Flow_{preop}$ was significantly higher in the CO group compared to the DASS patients (3.214 vs 1.784 l/min, $p<0.05$). $Flow_{preop}$ in two DASS patients was not obtained because of a short dialysis segment precluding positioning of two needles. Two patients did not receive a CVL, because high venous pressures in grossly dilated veins were thought an absolute contraindication for safe introduction and removal. In one patient the CVL was positioned incorrectly according to the postoperative chest radiograph, and his values of Sat_{ven} were omitted. Therefore, values of Sat_{ven} were available in 13 studies (CO n=6, DASS n=7). Complications associated with CVL introduction and removal were not observed. Measurements of $Flow_{us}$ were performed in all 16 studies. Determinations of P_{dig} were introduced at a later stage of the study and were available in a portion of the patients (CO n=5, DASS n=6).
The mean pre-operative systolic blood pressure in awake patients was 148 ± 8 mm Hg in the CO patients and 156 ± 20 in the DASS group (ns). In contrast intra-operative blood pressure during general anesthesia was only 106 ± 9 and 97 ± 6 mm Hg respectively. Correlations between $Flow_{preop}$ (or $Flow_{us}$), Sat_{ven} and P_{dig} just prior to banding were not significant in CO or DASS patients ($0.11<r<0.50$, all ns). In contrast, magnitudes of $Flow_{preop}$ and $Flow_{us}$ were significantly correlated ($r=0.60$, $p<0.05$).
Stepwise banding of the AVF significantly changed Sat_{ven} in all patients. Values in patients with CO dropped by -13% (93±2% (100% open AVF) vs 80±3% (closed AVF), $p<0.05$, figure 3). However, the fall in Sat_{ven} in patients with DASS was significantly smaller (-4%, 88±1% vs 84±2.%, $p<0.05$). In contrast, stepwise banding increased P_{dig} in patients with CO from 79±13 mm Hg (100% open AVF) to 102±9 mm Hg (closed AVF, p=0.02). A

	Cardiac overload (n=8)	DASS (n=8)
M/F	3/5	7/1
Age	51 ± 8	55 ± 8
Diabetes Mellitus (n)	0	2
Flowpreop (ml/min)	3214 ± 260	1784 ± 258*
Gracz (n)	6	5
Basilic transposition (n)	2	2
Ulnar-basilic transposition (n)	0	1

Table *Characteristics of study population*
*Sixteen studies were performed in 14 individuals. Patients with CO displayed a larger access flow compared to the DASS patients. *p<0.05 vs cardiac overload*

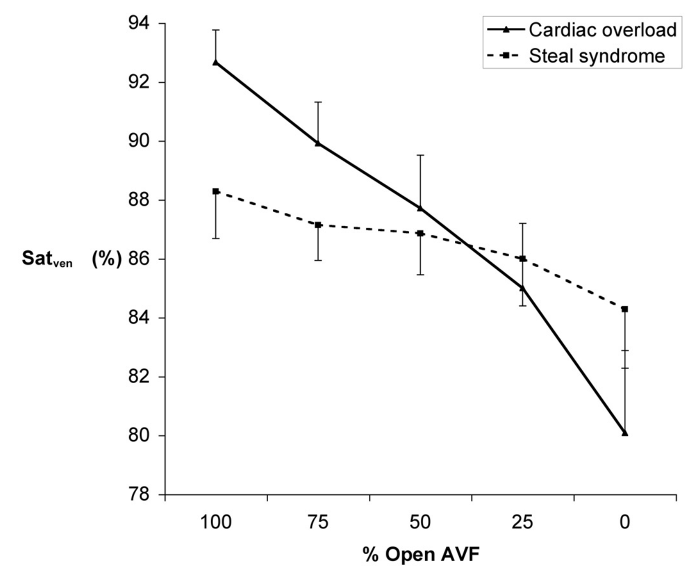

Figure 3 *The fall of venous saturation (Sat_{ven}) in patients with cardiac overload was significantly (P < .05) more pronounced compared with patients with dialysis access-associated steal syndrome. Data are presented as means ± standard error of the mean. AVF, Arteriovenous fistula.*

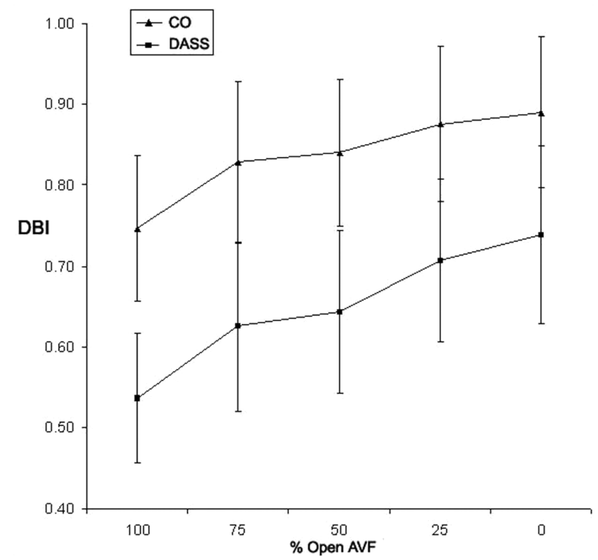

Figure 4 *Stepwise banding resulted in a similar increase in digital brachial index (DBI) in both cardiac overload (CO) and patients with dialysis access-associated steal syndrome (DASS) syndrome patients. Data are presented as means ± standard error of the mean.*

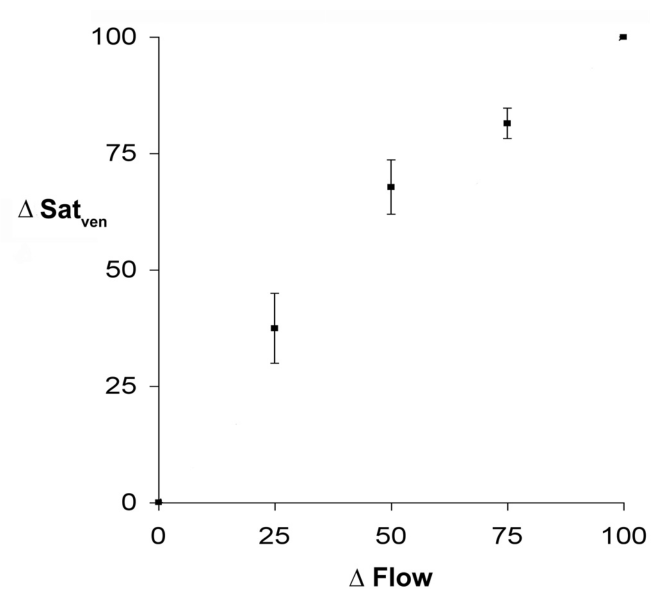

Figure 5 Correlation between alterations in venous saturation (Sat_{ven}) and access flow in patients with cardiac overload. The changes in flow are linearly related to changes in Sat_{ven}. Data are presented as means ± standard error of the mean.

similar 23 mm Hg increase was observed in patients with DASS (58±12 mmHg to 81±13 mmHg ($p<0.01$) In concert, DBI improved from 0.75±0.09 % to 0.89±0.09%) in patients with CO, and in patients with DASS from 0.54±0.08% to 0.74±0.11% (both $p<0.05$, figure 4). The magnitude of changes in access flow and Sat_{ven} were closely related, particularly in the CO patients ($r^2=0.96$, figure 5)

At the end of the banding procedure, access flow in patients with CO was still significantly lower ($p<0.01$) compared to prebanding values ($Flow_{us}$: -68±3%) as well as in patients with DASS ($Flow_{us}$: -56±7%). A decrease in venous saturations was also present in both groups (CO Sat_{ven}: -40±7%, $p<0.05$: DASS Sat_{ven}: -49±17%). Moreover, P_{dig} and DBI increased significantly ($p<0.05$) in patients with DASS (P_{dig} 58±12 mmHg to 74±13 mm Hg; DBI 0.54±0.08 to 0.72±0.10). In patients with CO, P_{dig} and DBI rose from 79±13 mm Hg to 96±13 mm Hg, and from 0.70±0.09 to 0.83±0.09, respectively.

DISCUSSION

Vascular surgeons are reluctant to perform surgery on an AVF in the presence of cardiac overload (CO) or hand ischemia (DASS, dialysis access-associated steal syndrome). This hesitance may in part be related to the paucity of useful intraoperative parameters guiding such corrective procedures. This approach is generally incorrect since persisting CO leads to increased mortality in the presence of a high-output AVF. Disconnection of an AVF in the presence of CO or DASS is to be avoided at all times. Therefore, modifying inappropriate access flow with maintainance of an adequate dialysis facility is the ultimate goal of any surgical procedure. Surgeons are in the need of finding techniques that can be used in the operating theatre to achieve these goals. The aim of the present study was to identify a set of objective parameters that reflects AVF flow in patients with access related CO or DASS.

Several authors have studied the feasibility of intraoperative monitoring techniques that can be used to correct high-output AVF's or DASS. Duplex monitoring of access flow and/or the bilateral subclavian arterial vasculature both aided in reducing flow in some patients (5,6). Others have successfully used digital oxygen saturation, angiodynography, photoplethysmography or pulse volume recordings in the treatment of patients with DASS (7-10). In general, most of these studies report on just a single aspect of the dysfunctioning AVF in relatively small groups of patients. A substantial portion of the reported techniques is hampered by suboptimal reproducibility and limited accuracy. Therefore, none of these intraoperative methods can be claimed as a gold standard of guiding corrective surgery.

Augmented fistula flows are intrinsically characterized by increased shunting of highly saturated arterial blood into the arm's venous vasculature. Values of central venous saturation may therefore be higher in patients harbouring an AVF when compared to healthy individuals. In one study central venous saturation in resting healthy subjects was 75% (range 69-78) (16). In contrast, mean saturation in our anesthetized dialysis patients (either CO or DASS) was much higher, with an open AVF (mean=91%), and even with a closed AVF (mean=84%). High levels of venous saturation in dialysis patients may be explained in several ways. The presence of an arteriovenous connection initially results in a locoregional hyperdynamic state, later on followed by compensatory adjustments in the cardiopulmonary system. Arterial structures in the arm will develop signs of hypertrophy including increased vessel diameter aimed at facilitating augmented arm flow. On the other hand, most dialysis patients do not use their shunt arms as intensive as the contralateral arm. Moreover, general anesthesiology is known for intensifying already low oxygen extraction rates. Therefore, high resting venous saturation levels in dialysis arms in this study are probably the combined result of a hyperdynamic state associated with low oxygen extraction rates due to inactivity and general anesthesiology. The largest drop in venous saturation following AVF clamping was found in CO patients, and this large fall is reflective of their hyperdynamic state.

Saturation levels in the subclavian vein were hypothesized to be related to volume of access flow. However, the correlation between preoperative access flow and venous saturation in the subclavian vein at the start of the operation appeared not significant.

This absence may be due to interindividual variation in cardiopulmonary function, blood pressure, peripheral vasculature, blood viscosity and AVF flow. By using an anesthesized individual as his/her own control, absent interindividual variability allows detailed study of access flow, digital pressures and venous saturation. Stepwise reduction of AVF flow resulted in significant alterations in saturation in the ipsilateral subclavian vein. Moreover, linearity was present between these parameters in patients with CO. This correlation was less obvious in DASS patients. In the latter group of patients the influence of confounding factors as mentioned earlier (e.g. blood pressure) may be more prominent and may interfere with the correlation between flow and saturation.
Continuous measurement of central venous saturation during banding requires the insertion of a CVL. The use of these lines is not advised by DOQI (14) because of the potential risk of venous stenosis and thrombosis. We observed no complications associated with a temporary 3 hour use of these lines. Long term complications are also thought negligible. For instance, there were no differences in patency of AVF's up to 4 years between patients who had a temporary CVL compared to patients without one (17). It is probably safe to use such temporary lines as they may potentially aid in banding procedures that are required for reducing cardiac overload.
Some authors have advised the intraoperative use of digital photoplethysmography as a monitoring technique during banding procedures in 'stealing' grafts. The AVF's were narrowed until a DBI of 0.6 or an absolute pressure of 50 mmHg was obtained (9). An almost linear relation was present between radial artery pressures and stricture length of the AVF vein during a surgically created stenosis of a transposed basilic AVF vein (18). In our study, digital pressures and DBI also increased following banding. The findings indicate that alterations in finger pressures, possibly in concert with alterations in Sat_{ven}, may be useful in modifying stealing AVF's. A randomized trial should clarify whether modifying AVF's using this approach is as effective as other techniques including DRIL-technique (19).
Are intraoperative flow measurements needed for corrective surgery in patients with CO or DASS? First of all, a physician has to decide which of these two clinical conditions prevails in his patient. If CO is the predominant factor, intraoperative alterations in venous saturation and access flow may both help in modifying access flow as they appear interrelated in these patients. If steal is dominant, one may use alterations in intraoperatively measured access flow as a basis for pushing the digital brachial index above the 0.6 value. Irrespective of the indication for correction (CO or DASS), access flow at the end of the procedure must always remain above its thrombotic threshold level.
In conclusion, narrowing an AVF during a banding procedure in patients with cardiac overload or digital ischemia leads to a dose dependent decrease in flow and venous saturation, whereas digital pressures increase. Alterations in these parameters have potential of guiding surgical correction of dysfunctioning AVF's in hemodialysis.

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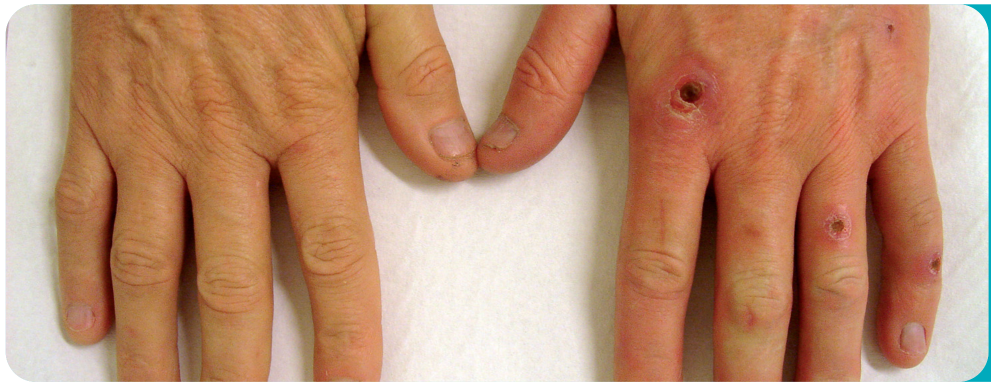
CHAPTER 6



Banding of hemodialysis access to treat hand ischemia or cardiac overload

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Seminars in Dialysis 2009; 22(2): 204-208

ABSTRACT

Introduction

A hemodialysis access may lead to cardiac overload (CO) or hand ischemia (HAIDI, hemodialysis access induced distal ischemia). Surgical banding restricts access flow and promotes distal perfusion. Aim of the study was to investigate short and long term clinical success of banding in these patient groups.

Methods

After evaluation using a standard protocol, banding procedures (n=19) were performed in patients (n=17) with a hemodialysis access flow ≥ 2 l /min or with refractory HAIDI. Various parameters including access flow, digital brachial index (DBI) and symptomatology of hand ischemia using a standard scoring system were determined before and after the operation.

Results

Surgical banding in CO patients (n=9) lowered access flows by 2 ltr ($Flow_{preop}$ 3.2 ± 0.3 l/min vs $Flow_{postop}$ 1.2 ± 0.1 l/min, p<0.001). Banding in HAIDI patients (n=10) increased DBI from 0.52 ± 0.08 to 0.65 ± 0.08 (p=0.05) whereas ischemic symptomatology was attenuated (153 ± 33 to 42 ± 15, p<0.02). All patients successfully continued dialysis, and immediate access occlusions (< 3 months) were not observed. Access flows remained at acceptable levels after a mean follow up of 30 months in surviving patients (n=11, Flow: 1.0 ± 0.1 l/min). Two patients were reoperated for recurrent CO (1 and 28 months postoperatively).

Conclusions

Surgical banding monitored by measurement of flow and finger pressures is an effective short and long term treatment modality for hemodialysis access related cardiac overload or distal ischemia.

INTRODUCTION

A minimal flow is required in a hemodialysis access if exchange of blood with the artificial kidney is to be successful (1). Flows initially increase after autogenous access construction but usually stabilize over time. In some patients however, flows may continue to increase possibly leading to cardiac overload (CO). Various surgical techniques have been proposed for the management of such a 'high-output' access including banding or revision of the anastomosis (2). Direct brachiocephalic accesses are at risk for the development of overload compared to a radiocephalic dialysis facility (3).
Hand ischemia (HAIDI, hemodialysis access induced distal ischemia) is an other potential complication associated with the presence of a dialysis access (4). Distal tissue oxygenation is diminished due to loss of perfusion pressure in the presence of a low resistance access. HAIDI is characterized by coldness, pain, cramps, altered sensibility and diminished strength in the ipsilateral hand. Diabetics are at risk for distal ischemia as collaterals may not sufficiently compensate for this loss of perfusion in the presence of distal occlusive disease (5). Some degree of HAIDI is routinely observed in a normal 'asymptomatic' dialysis population (6). Low digital finger pressures (P_{dig}) as determined by plethysmography are routinely observed in these patients. Access clamping leads to a substantial increase in P_{dig} (7).
Long term CO or intense hand ischemia not responding to conservative treatment require surgical correction. Distal revascularisation and interval ligation (DRIL) is proposed for the treatment of ischemia but the method may be less effective in cardiac overload (8). An alternative approach is creation of an artificial stenosis at the level of the anastomosis. The technique is termed 'banding' but the method was criticized as patency rates of banded access were dismal (9). Lack of objective parameters guiding banding may possibly explain the absence of enthousiasm in criticasters. Aim of the present study is to investigate the short term and long term efficacy of banding in patients with CO or HAIDI.

SUBJECTS AND METHODS

Study population

This pilot study was performed between March 2003 and January 2008 in the Máxima Medical Center (MMC), Veldhoven, The Netherlands. The MMC is a 865-bed community hospital serving a population of approximately 350.000 inhabitants. The study followed the Declaration of Helsinki for ethical research on human objects. The dialysis department accommodates 95 hemodialysis patients. Access flow in this population is measured every two months using standard dilutional techniques (HD01, Transonic Systems Inc, New York, USA) (10) as suggested by DOQI (1). Only patients with an arm access on chronic hemodialysis (> 3 months) qualified for study eligibility. Patients were

asked to participate if at least three consecutive access flows were ≥ 2.0 l/min, or if they experienced symptomatology of invalidating hand ischemia and objective signs of hypoperfusion (mottled skin, ulcers, low digital pressures). Conservative measures including application of warm dressings were unsuccessful. Potential patients were discussed in a team of vascular specialists including a nefrologist, a cardiologist, dialysis nurses and a vascular surgeon with special interest in dialysis surgery. If intervention was deemed necessary, individuals were informed on the nature of the study and its specifics and verbal and written permission was obtained. Patients were not studied if they refused (n=1) or if a language barrier was present (n=1).

Preoperative evaluation

Values of access flow (l/min) as determined in the month prior to operation by a two needle dilutional technique in the dialysis ward are termed $Flow_{preop}$. The upper threshold is 4 l/min as dictated by the Transonic device.
CO patients underwent an interview aimed at evaluating symptoms possibly related to CO, whereas an ischemic questionnaire was scored by patients with HAIDI in the presence of one of the nurses of the 'access-team'. An individual score quantifying hand ischemia was calculated as described earlier (6). In short, patients indicate severity (0, absent - 10, unbearable) and frequency (0, never – 10, always) of 5 symptoms associated with HAIDI (coldness, pain, diminished sensibility, strength, cramps). The minimal score in each of the 5 domains is 0 and maximal 100 points (10x10). All of these domain scores are added (Maximal score equals 5x100=500 points). Scores ranged from 35-50 in a group of 120 asymptomatic patients (6).
Physical examination included inspection, palpation and manual access occlusion according to a recent report (6). A cardiologist was consulted if deemed necessary and performed a trans-thoracic cardiac ultrasound in a portion of patients (n=13). All medication was recorded. If the patient's history and physical examination were consistent with HAIDI, visualisation of the arterial vasculature from aortic arch to digital arci was performed using a standard Seldinger angiography (11). All films were reviewed by a radiologist experienced in evaluating distal vasculature including hand arcades. A vascular laboratory technician performed photoplethysmography (PPG) aimed at determining systolic pressures (P_{dig}, in mm Hg) of the index finger of both hands (VasoGuard Nicolet, 8 Mhz, Scimed Ltd, Bristol, UK). An inflatable cuff was wrapped around the proximal phalanx of the index finger and the sensor was positioned on the palmar side of the distal phalanx. The digital brachial index (DBI) was calculated as the ratio of P_{dig} to systolic blood pressure. P_{dig} was also determined with open access and following manual compression of the access' venous outflow tract. This manoeuvre may abolish the loss of perfusion pressure due to the access, may reverse hypoperfusion and may predict successful corrective surgery.

Characteristics of operative set-up

Patients were operated the day after a dialysis session. Specifics of the operative procedure were recently reported (7). A central venous line (CVL, Central Venous Oximetry Catheter with AMC Thromboshield, Edwards Lifesciences, Irvine, USA) was positioned in the ipsilateral subclavian vein after induction of general anesthesia. The line's most distal port was considered in an optimal position if transport of blood through this port was effortless while proximal ports did not yield blood draws. This typical position of the CVL allows for measurements of venous saturation (Sat_{ven}) reflecting total arm values exclusively without contribution from jugular vasculature. A recent study found that access flow and Sat_{ven} are interrelated (7). Correct line placement was checked postoperatively using a chest rontgenogram. A PPG sensor for serial measurements was placed on the dialysis index finger. Oxygen saturation and blood pressure were measured noninvasively on the contralateral arm using standard techniques.

The access anastomosis including artery and vein was dissected. An additional 1.5 cm incision approximately 10-15 cm downstream towards the axilla was used to identify a second portion of the access' outflow tract. The space between vein and a 4-8 mm flow probe was filled with acoustic gel and this site was used for continuous measurements of access flow ($Flow_{us}$, l/min) using a transit time technique (HT313, Transonic Systems Inc, New York, USA). A 5 mm wide flat woven polyester band (Mersilene, Johnson & Johnson, Hamburg, Germany) was loosely wrapped around the vein 1-3 cm's from the anastomosis. The loose ends of the band were positioned into a specially designed pulling mechanism allowing narrowing of the venous outflow tract ('banding') in a controlled manner. Both puller and flow probe were held by a metal rod fixed to the table. This setup resulted in total absence of movement artefacts and optimal measurements. All banding procedures were performed by one surgeon (MS) and one anesthesiologist (ML).

Measurement protocols

Two separate protocols were used. If banding was indicated for CO, the goals were to reduce access flow down to 1.0-1.2 l/min and to attain a reduction in Sat_{ven} (7). Measurements were started if a stable signal of $Flow_{us}$ with >90% accuracy was attained (HT331, Transonic Systems Inc, New York, USA). Maximal and minimal values of $Flow_{us}$, Sat_{ven} and P_{dig} were determined with a 100% open access, and during clamping of the access' outflow tract (0% open). In order to calculate the desired reduction of access flow, two assumptions were made. Firstly, $Flow_{us}$ accurately reflects $Flow_{preop}$. Secondly, narrowing of the access' venous leg with concomitant decrease in $Flow_{us}$ results in proportional decrease of $Flow_{preop}$. The following example in a female patient with CO illustrates the way her desired access flow was calculated. $Flow_{preop}$ was 3.6 l/min. Her desired access flow was set at 1.2 l/min which is equal to 33% of her $Flow_{preop}$. The intraoperative $Flow_{us}$ appeared only 1.5 l/min. This large difference between $Flow_{preop}$ and $Flow_{us}$ is thought the result of low systemic blood pressures during general anaesthesiology. Therefore, the

access was banded at 33% of the $Flow_{us}$ being 1.5 x 0.33 = 0.50 l/min. Similar calculations were utilized in the remainder of the CO population.

If banding was required for HAIDI, the aim was to obtain a substantial increase in DBI, preferably in excess to 0.6 (12) while flow was to be maintained well above the access' thrombotic threshold level (> 400 ml/min). Apart from these objective values, maintenance of thrill, return of distal pulses as well as improved hand color were also checked intraoperatively. When the combined readings of $Flow_{us}$ and P_{dig} as well as results of inspection of the hand were satisfactory, the position of the band was secured using a metal clip that was secured with prolene sutures. The bands loose ends were cut, and the incision was closed in two layers. Patients were allowed to undergo hemodialysis using the banded facility as scheduled. Access flow was determined one week postoperatively using a two needle dilutional technique in the dialysis ward ($Flow_{postop}$). Ischemic symptomatology scores were obtained in the second postoperative week. Various other data were tabulated including time (months) between initial construction of access and banding, and amputation rate (< 3 months post banding). Access flow (l/min) and mortality were also determined at the end of the 58-month study period.

STATISTICAL ANALYSIS

The significance of changes in various parameters were calculated using paired t-tests. Differences between mean values were calculated using one- or two-sided unpaired t-tests. Results were expressed as mean ± s.e.m. A $p < 0.05$ was considered significant.

RESULTS

General

Patients (n=17) were on chronic hemodialysis because of congenital kidney disorders (n=4), hemolytic uremic syndrome (n=2), diabetes mellitus (n=2), chronic glomerulonefritis (n=2), postrenal diseases (n=2), hypertension (n=2), glomerulosclerosis (n=2), and tubular necrosis following aneurysm repair (n=1). Patients with CO were substantially longer on dialysis (87 ± 19 months) compared to patients with HAIDI (23 ± 6, p<0.02).

Three types of direct access were banded, side-to-end brachiocephalic access (n=12), upper arm basilic transpositions (n=4), and one lower arm ulnarbasilic access. Patient characteristics are depicted in table 1. Banding was performed because of CO (n=9) and hand ischemia (n=10). Data represent 19 studies in 17 individuals as two patients were studied twice. The two diabetic patients were suffering from hand ischemia. Mean ejection fraction in CO patients (n=7) was substantially lower (51 ± 2%) compared to the ischemic group (n=6, 73 ± 9 %, p<0.001). However, number of cardiac medication was not different between the two populations (data not shown). Angiographies were performed in all patients with hand ischemia (n=10). Subclavian or axillary arterial stenoses were not observed. One nondiabetic patient demonstrated a severely sclerotic radial artery. A second nondiabetic patient had an occluded ulnar artery. Three patients (one diabetic) displayed insufficient superficial or deep hand arcades. Hand arcades were unjudgable in the remaining patients (n=5), as the contrast medium was immediately shunted into the access. Separate runs while manually closing the access aimed at visualisation of lower arm vessels were not performed.

Banding in CO patients

$Flow_{preop}$ in patients with CO was approximately 1.2 liter more compared to the population with hand ischemia (3.2 ± 0.3 l/min vs 2.0 ± 0.3 l/min, p<0.001). Banding diminished access flow from 3.2 ± 0.3 ml/min to 1.2 ± 0.1 ml/min (p<0.001, figure 1).

Banding in HAIDI patients

DBI in these patients increased from 0.52 ± 0.08 to 0.65 ± 0.08 (p=0.05) (figure 2). Access flow decreased from 2.0 ± 0.3 l/min to 1.3 ± 0.3 l/min. Ischemic symptomatology as evaluated by the questionnaire diminished from 153 ± 33 to 42 ± 15 (p<0.02). A portion of the questionnaire data is presented in table 2. Pain in particular was virtually abolished by banding. Ischemic ulcers in two patients healed after surgery (figure 3).

	CO (n=8)	Hand ischemia (n=9)	p
Male (n)	3	7	n.s.
Age (yrs)	51 ± 8	59 ± 7	n.s.
Diabetes (n)	0	2	n.s.
Atherosclerosis (n)	3	5	n.s.
Hypertension (n)	5	3	n.s.
Hypercholesterolemia (n)	1	1	n.s.
Cigarette smoking (n)	1	3	n.s.

Table 1 Characteristics of patients with a direct hemodialysis access undergoing banding because of cardiac overload or hand ischemia.

	Before	After	p =
Cold sensation	50 ± 9	12 ± 8	0.01
Pain	23 ± 10	2 ± 2	0.059
Sensibility	35 ± 13	12 ± 7	0.177
Strength	42 ± 14	15 ± 11	0.094
Cramps	3 ± 2	1 ± 1	0.64

Table 2 Symptomatology of hand ischemia quantified by a questionnaire before and after surgical correction using banding (n=10 patients). Value for each symptom is calculated as: Severity (Visual Analogue Scale: 0 (absent) - 10 (unbearable) x Frequency (Visual Analogue Scale: 0 (never) - 10 (constant); maximal value is 100.[6]

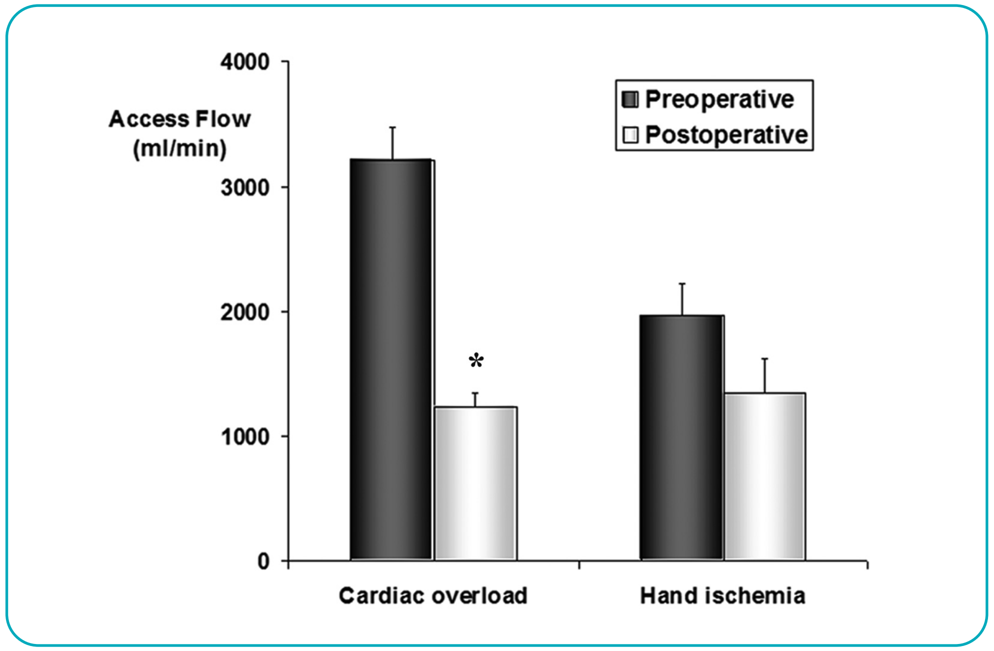

Figure 1 Access flow before and after banding for cardiac overload or hand ischemia using a combination of flow monitoring, venous saturation and digital pressures (p<0.001).*

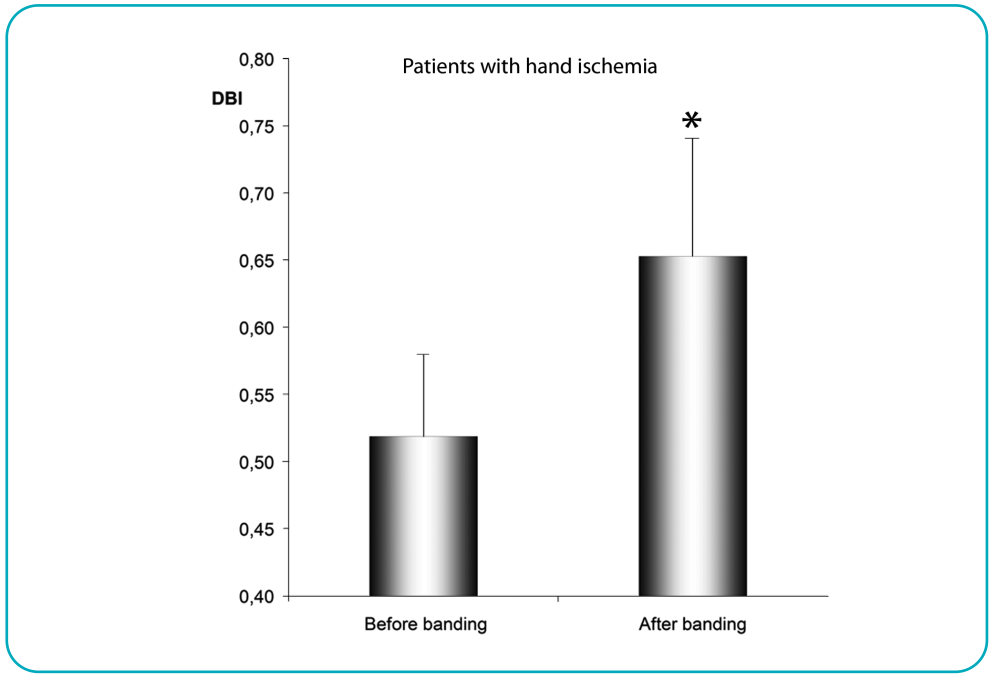

Figure 2 DBI (digital brachial index) in patients with hand ischemia before and after banding (p=0.05).*

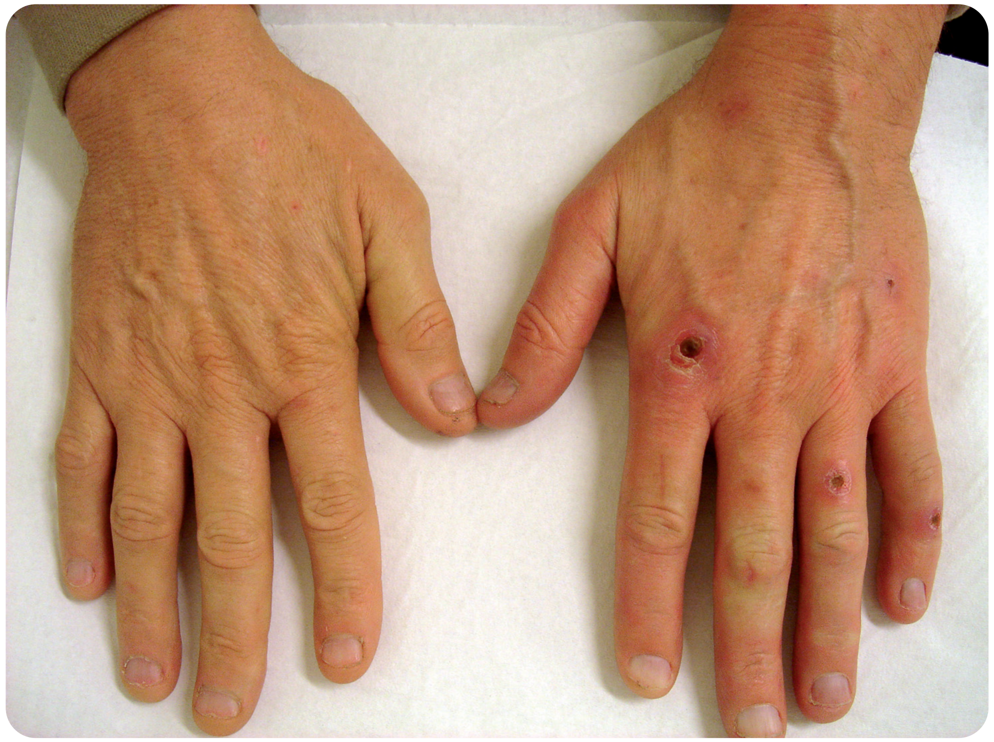

Figure 3 Ischemic ulcers in a patient with an elbow access (flow 1.1 ltr/min) and low digital pressures (42 mm Hg). Following banding, ulcers healed after 3 months.

Complications and Follow-up

Complications including wound infections were not observed. Operative morbidity and mortality were absent. All patients were discharged as scheduled. No patient required an amputation in the three months postoperative period. All patients successfully continued dialysis immediately after banding, and all accesses remained patent postoperatively (< 3 months).

Our first study patient was banded in March 2003 but required a second banding in July 2005 because of recurrent CO > 2 l/min. Her present flow (November 2007) is 1.1 ltr/min. Results of one procedure in our ninth study patient with CO were unsatisfactory, and banding was repeated one month later. His present flow is 1.5 ltr/min. At the end of the 58-months study period, access flow was 1.0 ± 0.1 l/min in surviving patients (n=11).

DISCUSSION

The number of direct elbow access is rising at the expense of wrist access due to an increased percentage of patients suffering from obesity and diabetes mellitus. The down side of superior patency rates (13) and a longer lifespan of a direct elbow access is the occurrence of long term complications such as cardiac overload following prolonged high access flows (> 2 l/min) (2). Cardiac failure may ensue possibly contributing to relatively high mortality rates in a dialysis population. Interestingly, patients with CO were 5.5 years longer on dialysis compared to HAIDI patients. This prolonged time period of overload may have diminished cardiac function as ejection fraction was 22% lower in the CO group compared to HAIDI patients (CO: 51± 2%, HAIDI: 73± 9%).

Hypoperfusion of distal tissue (HAIDI) is an other complication incidentally associated with the presence of an ipsilateral elbow access (4). Reversal of blood flow ('steal') is by many wrongly incrimated in the pathophysiology of this type of ischemia. However, it must be understood that ischemic symptomatology is due to loss of perfusion pressure in the presence of an dialysis access. Several conditions including diabetes, atherosclerosis and hyperparathyroidism may mimic or worsen hand hypoperfusion. The rise in elbow hemodialysis facilities in the coming decades calls for further refinement of management strategies aimed at treating complications such as cardiac failure and HAIDI associated with this type of access.

HAIDI or even tissue loss due to a homolateral hemodialysis access mandates angiographic evaluation. Stenotic lesions of inflow tract require endovascular correction. If these and other conservative measures fail, vascular surgery may be indicated. Some surgeons favour a distal revascularization interval ligation (DRIL) for treatment of ischemia. Access flow is claimed to remain unaltered while the ischemic hand is revascularized using a bridge bypass overspanning the access' arteriovenous anastomosis (8). A recent study reported a 90% success rate following DRIL in 52 patients (14). A potential disadvantage of the technique is the construction of a bypass with associated risk of thrombosis although limb loss is not observed. A second promising technique for treatment of HAIDI is proximalization of arterial inflow (PAI) (15). After access disconnection close to the anastomosis, inflow is again instituted using a small caliber PTFE graft originating from a more proximal portion of the artery with a higher capacity. PAI is a physiological method for treatment of distal ischemia as native arteries are left undisturbed.

An alternative surgical technique for the correction of HAIDI is termed banding. The efficacy of this method is questioned as parameters guiding surgery are scarse. A recent study found that banding of an access had profound effect on P_{dig} (7). The purpose of the present study was to investigate whether ischemic symptoms in hemodialysis patients could be abolished by banding. The results indicate that DBI in these patients increased from 0.52 to 0.65. These augmented DBI's were associated with attenuated ischemic symptomatology (153 ± 33 to 42 ±15) using a previously published ischemic questionnaire. Interestingly, mean postoperative scores of 42 are not different from values observed in an asymptomatic reference population (range 35-50) (6). For instance, levels of pain and coolness diminished about 10-fold following banding. Banding guided by plethysmography appears effective in attenuating ischemic symptoms while pushing DBI values above the 0.6-level, a cut-off point that is associated with severe hand hypoperfusion (12). The present study also hypothesized that cardiac overload due to a hemodialysis access was correctable using the banding technique. Banding in general is surrounded by scepsis (9) although others express faith in this technique (16,17). Some fear an increased risk of access thrombosis or insufficient flow reduction. One study reported that intraoperative access flow measurements aided in determining degree of banding for this indication (18). In the present study access flow in CO patients was reduced from 3.2 l/min to 1.2 l/min. Moreover, flows remained within an acceptable range during the 28-month observation period. Banding for cardiac overload guided by intraoperative monitoring of access flow is effective on both the short and the long term.

Access flow was measured using two different techniques, preoperatively by dilution, and intraoperatively using ultrasound. Flows determined by dilution were considerably higher when compared to ultrasound. This apparent discrepancy is most probably related to differences in systemic blood pressures. Mean blood systolic pressure in an anesthetized patient during banding was only 111 ± 8 mm Hg, whereas these values were 153 ± 10 mm Hg in an awake patient undergoing flow measurements using a two-needle technique in the dialysis ward. This difference may be less if surgery is performed using locoregional anaesthesiology although this latter technique may greatly influence flow characteristics in the arm's vasculature (19). Alternatively, one may administer inotropic medication during general anaesthesiology aimed at increasing systemic pressures towards normal values.

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CHAPTER 7

Time of onset in Hemodialysis Access-Induced Distal Ischemia (HAIDI) is related to access type

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ABSTRACT

Background

A small portion of hemodialysis patients develops hand ischemia (HAIDI, hemodialysis access induced distal ischemia) in the presence of an arteriovenous fistula (AVF). It is unknown if time of onset of ischemia is related to type of AVF. Aim of the review is to investigate if a relationship is present between type of AVF and time of onset and intensity of HAIDI.

Methods

Standard databases and reference lists of pertinent literature were systematically searched. HAIDI was classified as 'acute' (<24 hours after routine access construction), subacute (within one month), or chronic (>one month). Location, type and follow up of AVF were tabulated.

Results

Twenty-one studies reporting on surgically or percutaneously corrected HAIDI patients (n=464) fulfilled the inclusion criteria. Acute HAIDI strongly (88%) correlated with non-autogenous AVF. In contrast, chronic HAIDI was predominantly (91%) observed following autogenous AVF based on the cubital segment of the brachial artery. A simple clinical classification for chronic HAIDI guiding treatment strategies is proposed.

Conclusions

Hand ischemia occurring early after routine access surgery is usually related to grafts and not to autogenous access construction. If patients have several risk factors for acute hand ischemia (diabetes), nephrologists and vascular surgeons may choose an autogenous AVF. A disadvantage of an autogenous access is its association with chronic hand ischemia, particularly if constructed with a brachial artery.

INTRODUCTION

An arteriovenous fistula (AVF) does not compromise hand perfusion in the majority of hemodialysis patients. Nevertheless, about 5% develops ipsilateral hand ischemia, recently termed 'hemodialysis access induced distal ischemia' (HAIDI) (1). Various patterns of HAIDI may be identified. An acute form of HAIDI occurs within hours after routine access surgery and is characterized by total loss of hand function. This vascular emergency mandates urgent correction as ischemic sequelae are irreversible after some hours (2). However, most dialysis patients eventually requiring invasive management for HAIDI develop ischemic symptoms over weeks to months (3), or even 20 years after AVF creation (4). Chronic hand ischemia is often mild, but prolonged severe hypoperfusion leads to tissue necrosis necessitating amputation of fingers, hand or even a forearm in about 1% of patients (5) (figure 1-4).
In the coming decade, the incidence of chronic HAIDI is expected to rise due to the recent popularization of autogenous elbow AVF's (6-7). Moreover, ongoing maturation of elbow AVF's in aging dialysis populations with progressively diminished arterial conductivity as well as increased awareness of care providers likely contribute to larger numbers of HAIDI patients receiving treatment. Several issues on HAIDI are subject to debate. Firstly, it is not clear if type of AVF determines time of onset of hand ischemia. One study incorporating 28 patients suggested that HAIDI occurring early postoperatively is associated with graft insertion, whereas ischemia that developes later on is usually caused by an autogenous AVF (8). Secondly, a simple and practical classification for HAIDI is lacking although reporting on arteriovenous hemodialysis accesses has been standardized (7,9). Some authors classified HAIDI based on time of onset after AVF construction using an arbitrary one-month cut-off point ('early' versus 'late'), while others characterized HAIDI based on a combination of signs and symptomatology (10-11), or emphasized on clinical patterns and associated therapy (12). A classification of HAIDI should be simple to memorize, should incorporate defined signs and symptoms and should be able to direct treatment strategy.
Aim of the review is to investigate if a relationship is present between type of AVF and time of onset of HAIDI. Furthermore, a simple classification (analogous to Fontaine's grading of lower limb ischemia) for chronic HAIDI will be proposed, based on well-known clinical criteria for severity of distal ischemia.

METHODS

Data bases including PUBMED and Google were searched using the terms hemodialysis, digital, hand ischemia, arteriovenous fistula (AVF), arteriovenous access, graft, steal, ARI (access related ischemia), DASS (dialysis associated steal syndrome), HAIDI (hemodialysis access induced distal ischemia), percutaneous balloon angioplasty,

Figure 1 *Chronic hemodialysis access induced distal ischemia (HAIDI). Dry necrosis of top of thumb.*

Figure 2 *Chronic HAIDI. Painful ulcers on dorsal aspect of fifth finger.*

Figure 3 *Chronic hypoperfusion 18 months after insertion of an autogenous elbow AVF resulted in amputation of several fingers of the left hand.*

Figure 4 *Uncontrollable sepsis and hand amputation in a patient despite a ligated elbow AVF.*

intravascular stent insertion, intravascular coil insertion, Miller procedure, banding, DRIL (distal revascularization-interval ligation) and PAI (proximalization arterial inflow,) in combinations with the Boolean operators AND and OR. Reference lists of articles reported between January 1966 and January 2009 were checked for pertinent literature.

A publication qualified for analysis if

1 it reported on chronic hemodialysis patients receiving a correction using a surgical or percutaneous technique for HAIDI, and
2 included at least 5 operated individuals, and
3 reported type (graft, autogenous) and position (wrist, elbow, upper arm) of access as well as
4 time of onset of ischemia (immediately, within the fist postoperative month, or >1 month) after construction of that specific access.

Time of onset of HAIDI was defined as 'acute', 'subacute' and 'chronic'. HAIDI was considered 'acute' when patients were reoperated within one day after routine AVF insertion. Most authors described this type of postoperative ischemia as 'immediate'. Ischemia requiring correction within the first postoperative month but later than 24 hours after the first operation was termed 'subacute', and after one month 'chronic'. Data were expressed as mean ± sem.

RESULTS

The search identified 90 reports, of which 21 fulfilled all 4 inclusion criteria. Sixty-nine reports were not eligible for study (< 5 patients, n=45; access position or type not reported, n=3; time of onset of ischemia in relation to access not specified, n=21). Table 1 summarizes data from these 21 studies on patients (n=464) undergoing correction for all three types of HAIDI (2,8,11-29). Acute ischemia was diagnosed in 22% (104/464). The majority of these acute patients (87%, 91/104) had received a nonautogenous AVF whereas only a small portion of patients (13%, 13/104) had undergone an autogenous elbow AVF construction. In contrast, patients who were operated later on in the first postoperative month for subacute HAIDI (97/464, 21%) predominantly harboured an autogenous elbow AVF (79%, 77/97) compared to 21% (20/97) with a graft AVF.
A total of 263 patients (57%) received surgery or a percutaneous correction for chronic HAIDI some 16±3 months after the initial AVF construction. Of these chronic patients, 88% (232/263) had an autogenous AVF compared to 12% with a graft (31/263). Chronic HAIDI was seldomly associated with an access at wrist level (9%, 20/232) compared to elbow level (91%, 212/232).

Author	Year	Patient	Acute (< 1 day)	Subacute (< 1 month)	Graft			Direct (e/w)	Chronic (> 1 month)	Graft			Direct (e/w)	Months after Access
					Upper arm tube	Loop	Leg			Upper arm tube	Loop	Leg		
Surgical														
Odland (13)	1991	16	12	0	0	12*	0	0	4	0	4*	0	0	n.r.
Schanzer (14)	1992	14	10	0	10	0	0	0	4	2	0	0	2 (1/1)	32
Haimov (15)	1996	34	27	0	27	0	0	0	7	2	0	0	5 (4/1)	36
Katz (16)	1996	6	4	0	3	1	0	0	2	0	0	0	2 (2/0)	3
Berman (17)	1997	21	0	10	1	3	3	3 (2/1)	11	0	2*	0	9 (8/1)	n.r.
Stierli (18)	1998	6	0	0	0	0	0	0	6	0	0	0	6 (6/0)	5
Lazarides (2)	1998	8	7	0	7	0	0	0	1	0	1	0	0	1
Lin (19)	1999	14	6	3	3	6	0	0	5	0	0	0	5 (5/0)	n.r.
Korzets (20)	2003	9	5	2	5	1	1	0	2	0	0	0	2 (2/0)	6
Lazarides (8)	2003	28	18	0	17	1	0	0	10	0	0	0	10 (10/0)	6
Ozisik (21)	2003	6	2	2	0	0	0	3/1	2	0	0	0	2 (1/1)	8
Sessa (22)	2004	18	0	6	0	0	0	6 (6/0)	12	0	0	0	12 (10/2)	8
Illig (23)	2005	9	1	1	0	0	0	2 (2/0)	7	0	0	0	7 (7/0)	15
Zanow (24)	2006	78	0	7	0	6*	0	1 (1/0)	71	0	10*	0	61 (51/10)	24
Walz (25)	2007	36	0	13	0	0	0	13 (13/0)	23	0	0	0	23 (23/0)	8
Therman (12)	2008	63	0	29	0	0	0	29 (23/6)	34	0	0	0	34 (30/4)	12
Huber (11)	2008	64	12	24	0	2	0	34 (34/0)	28	0	0	0	28 (28/0)	n.r
Yaghoubian (26)	2009	7	0	0	0	0	0	0	7	0	0	0	7(7/0)	27
Percutaneous														
Guerra (27)	2002	10	0	0	0	0	0	0	10	3	2	0	5 (5/0)	10
Asif (28)	2006	12	0	0	0	0	0	0	12	0	4	0	8 (8/0)	8
Kariya (29)	2009	5	0	0	0	0	0	0	5	0	1	0	4 (4/0)	17
Total		**464**	**104**	**97**	**73**	**32**	**4**	**92 (84/8)**	**263**	**7**	**24**	**0**	**232 (212/20)**	
%		**100**	**22**	**21**					**57**					
mean														**16±3**

Table 1 Type of HAIDI in relation to access.

*Numbers represent procedures. * = subdivision is not provided. n.r. not reported. e/w=elbow/wrist*

DISCUSSION

The present analysis of published HAIDI populations undergoing a surgical or a percutaneous correction indicates that time of onset of hand ischemia is related to type of access. Acute HAIDI (<1 day) is strongly correlated with nonautogenous AVF's constructed with the brachial artery in the cubital region. In contrast, subacute HAIDI (first month, but beyond 1 day) was observed 4 times more frequently with autogenous AVF's compared to grafts. Chronic HAIDI (>1 month) is strongly correlated with a maturing autogenous AVF in the elbow region. A seemingly higher incidence of chronic ischemia in more recent series relative to acute ischemia may reflect the increased popularization of autogenous elbow AVF's.

The clinical spectrum of ischemia following routine AV access surgery is diverse. In its most extreme form, it is noticed at the end of (or immediately after) the operation as intense pain, paleness and paralysis of the hand. Although rare, its phenomenology is characteristically reflecting profound ischemia and the diagnosis is simple (2). This untoward event mandates immediate corrective surgery. This condition is appropriately described as 'acute HAIDI'.

Apart from this acute form of HAIDI, a separate neuropathic entity related to local arterial hypoperfusion may also occur within some hours after construction of an AVF at elbow level. This condition termed ischemic monomelic neuropathy (IMN) is caused by focal ischemic axonal nerve injury involving sensory and motor branches in distal parts of limbs (30). Characteristically, the syndrome occurs in diabetics after elbow access surgery. Signs of peripheral hypoperfusion (cold skin, diminished radial pulsations, low digital pressures) may be entirely absent (31-32). Immediate reintervention (either AVF ligation or diminishing anastomotic area) aimed at increasing locoregional perfusion pressure may reverse this condition (2,33). Urgent consultation of a surgeon is crucial as neurological damage is irreversible after some hours. IMN is due to severe hypoperfusion of segments of median, ulnar or radial nerves located in the elbow region. We hypothesize that creation of an AVF with the brachial artery may have diminished perfusion pressure in neighbouring side branches feeding these nerve segments. IMN is considered a special form of acute HAIDI although it is proximally located and associated with neurological dysfunctioning exclusively.

The present review demonstrates that less than a quarter (22%) of all patients was operated for acute HAIDI, whereas some additional 21% underwent surgery for subacute HAIDI. The one month interval has been (arbitrarily) introduced in the literature and may possibly reflect the natural history of this subacute form of HAIDI. However, several pathophysiological mechanisms leading to subacute ischemia may be identified in this heterogenous population. For instance, this group may contain patients with an acute form of HAIDI but operative treatment could be delayed more or less safely since vitality of tissues was not immediately threatened and patients could cope with the ischemic symptoms. Moreover, this subacute group may also contain patients with distal ischemia following fast maturation of the arteriovenous anastomosis and efferent veins in the absence of compensatory maturation of the afferent arteries. Distal ischemia may also have occurred after rapid development of stenotic lesions in the arterial tree. Patient's as well as doctor's delay in acute ischemia probably also explain some of the cases in this subacute group.

Over half of all patients (57%) with HAIDI develop this condition gradually over time and require surgery or a percutaneous correction after a mean of 16±3 months following the initial access construction. Due to its slow development, the clinical picture of chronic HAIDI is far less conspicuous compared to the acute form. Patients may initially experience minor symptoms of arm claudication, or slight pain during dialysis or intense use of the hand. When the disequilibrium between nutritive perfusion and metabolic demands of tissues progresses, pain may be experienced during rest or in between dialysis treatment sessions (7). The syndrome of chronic HAIDI may partially be caused by increasing access flows due to disproportional 'maturation'. Maturation is a term which is used to describe progressive dilating (or positive) remodelling of vascular structures associated with the AVF including afferent arteries, the arteriovenous anastomosis and efferent veins induced by constantly increasing blood velocities in these vessels (34,35). In some patients, notably with diabetes and atherosclerosis, positive remodelling of arteries is hampered while veins of the fistulous complex progressively dilate. These simultaneously occurring events will result in a progressive decrease of the access' resistance. As a consequence, augmented access flows through relatively resistant afferent arteries lead to an ongoing lowering of mean arterial pressures and less effective distal tissue perfusion (36,37). Recurrent periods of uremia (38) and hypotension after dialysis both facilitate additional distal trombosis (17). Aging per se, characteristically inducing progressive arteriosclerosis associated with hardening and stenosing of the arterial walls, likely adds to progressive HAIDI over time. The relative contribution of these pathophysiological phenomena to the severity of chronic HAIDI is unknown.

As the onset of chronic hand ischemia is multifactorial, it is impossible to predict distal hypoperfusion in a patient scheduled for routine access surgery. However, the likelihood of developing HAIDI is thought proportional to number of risk factors (39). A hypothetical 60-year old diabetic female with a history of previous access procedures scheduled for an upper arm graft originating from the cubital brachial artery is more at risk for developing a severe form of HAIDI compared to a 20-year-old male receiving his first autogenous radial-cephalic access. Onset of HAIDI in the female is more likely if the preoperative digital-brachial systolic pressure index (DBI) is <1.0 (normal: >1.0)(40), or if intraoperative DBI immediately after access opening drops below 0.6, or even below 0.4 (41). However, positive predictive values of these DBI's were low. A preoperative Allen test is unreliable since nearly all patients eventually requiring surgery for HAIDI demonstrated normal results. Loss of preoperatively palpable radial arterial pulses

immediately after access construction appeared an ominous sign (42). Nephrologists and surgeons must preoperatively discuss types of HAIDI with their patients if two or more risk factors including diabetes mellitus, female gender, hypertension, coronary artery disease, peripheral arterial disease, current smoking and multiple previous ipsilateral access procedures are present (39). Autogenous AVF's located at wrist or elbow level remain first choice. If veins are not available, one may consider to connect a graft to a portion of an artery that is more proximal than cubital level. These upper arm or axillar arteries have sufficient capacity and are in theory (35,43) and in daily practice (24,44) not associated with distal ischemic events.
The natural history of chronic HAIDI appears analogous to the sequence of events that is observed in the progression of peripheral obstructive arterial disease (PAOD) of the lower limbs. In Fontaine's first phase, PAOD of the lower limbs is asymptomatic but discrete signs of diminished perfusion following arterial obstructions may occasionally be observed objectively. If disease progresses or functional demands increase, intermittent claudication may occur during brisk walking and later on during normal walking (Fontaine stadium 2). More severe disease will lead to ischemic pain in resting conditions (Fontaine 3). The fourth stadium is characterized by tissue loss. This Fontaine classification reflects a progressive disequilibrium between requirements and availability of tissue perfusion and is universally accepted because of its simplicity and reproducibility. Stadium 2 of Fontaine is usually subdivided into 2a (non-invalidating claudication) and 2b (invalidating claudication). Some found it useful to subdivide stadium 4 into 4a (limited tissue loss, successful revascularisation leads to a functional foot), and 4b (successful revascularisation improbable). For chronic HAIDI, we propose an analogous classification including symptoms, signs and an therapeutic approach for each stage.

HAIDI grade 1
No clear symptoms but discrete signs of mild ischemia may be observed (slight cyanosis of nail beds, mild coldness of skin of hand, reduced arterial pulsations at the wrist, reduced systolic finger pressures). Conservative treatment may be indicated.

HAIDI grade 2a
Complaints during dialysis sessions or intense use of the hand: tolerable pain, cramps, paresthesias, numbness or disturbing coldness in fingers or hand. Conservative treatment is indicated.

HAIDI grade 2b
Complaints during dialysis sessions or use of the hand: intolerable pain, cramps, paresthesias, numbness or disturbing coldness in fingers or hand. A combined treatment including conservative and invasive treatment (endovascular or surgical) is indicated.

HAIDI grade 3
Rest pain or motoric dysfunction of fingers or hand. Urgent invasive treatment supported by conservative measures is indicated.

HAIDI grade 4a
Limited tissue loss (ulceration, necrosis). Clinically significant hand function will probably result if ischemia is reversed. Urgent invasive treatment supported by conservative measures is indicated.

HAIDI grade 4b
Irreversible tissue loss of the hand or proximal parts of the extremity. Impossibility to preserve clinically significant hand function. Amputation is required.

The present classification facilitates comparison of severity of chronic HAIDI among hemodialysis populations, aids in defining the necessity of various treatment options and allows evaluation of treatment efficacy.
Initial treatment of chronic HAIDI should be guided by its severity and may include a combination of conservative measures such as warm hand dressings, reduction of antihypertensive agents, hand exercise and vasospastic medication (45). If such conservative measures fail, catheter-based therapies may optimize arterial inflow in the presence of stenotic lesions in any of the afferent arteries (27-29) (figure 5).

Figure 5 Angiogram of a patient with hand ischemia in the presence of an occluded subclavian artery. A percutaneous transluminal angioplasty abolished ischemic symptoms.

Surgical consultation should be considered if conservative and endovascular approaches fail. Surgeons may advise access ligation (if another access facility is present) in the absence of inflow lesions, or when ischemic symptoms are not abolished after successful endovascular treatment. If invasive treatment is required and the access flow is >1.0-1.2 liter/min, a banding procedure is simple and effective on the short and long term (46). More invasive techniques include distal revascularization-interval ligation (14) or altering inflow site (24, 47) may be used if access flows are below this threshold.

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CHAPTER 8

Retarded hand growth due to a hemodialysis fistula in a young girl

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ABSTRACT

Long term presence of an arteriovenous hemodialysis fistula (AVF) may lead to alterations in hand perfusion. A 14 year old girl developed pain associated with hand ischemia 5 years after a successful kidney transplantation. When she was eight years old, she required a period of hemodialysis using an autogenous left upper arm AVF. Compared to the healthy right hand, a smaller ischemic left hand was observed in the presence of a patent AVF. Access flow was 1400 ml/min. Seldinger angiography demonstrated a stenotic brachial artery, and reversed blood flow in the radial artery was found by Duplex measurements. AVF ligation abolished the ischemic symptoms. Distal hypotension due to an impaired arterial inflow combined with a low resistance elbow AVF may result in chronic hypoperfusion of acral portions of the extremity and growth retardation. In children with an optimal renal transplant function and a patent elbow AVF suffering from lowered distal tissue perfusion, access ligation is advised.

INTRODUCTION

End stage renal disease in early childhood is rare. Some children may have to undergo hemodialysis using an arteriovenous fistula (AVF) prior to kidney transplantation. Access related long term complications including high flow or hemodialysis access induced distal ischemia (HAIDI) are uncommon in young populations (1). A large study evaluating 434 accesses in children demonstrated a 9% HAIDI rate whereas high access flow was present in just 1% (2).
Alterations in limb morphology in the presence of an AVF are also exceedingly rare. One 9-year old child with multiple accesses in both arms was found to have upper limbs of different length (2). If asymmetry in legs is observed, the dialysis limb is usually the largest (3).
We present a 14 year old girl with symptomatic hand ischemia due to a patent brachio-cephalic AVF several years after a successful kidney transplantation. Surprisingly, a substantially smaller ischemic left hand was observed in the presence of well developed upper arm AVF. A brachial artery feeding the access appeared stenotic. AVF ligation reversed the hand ischemia. A low resistance elbow AVF combined with diminished arterial inflow may jeopardize distal limb perfusion and result in growth retardation. Access ligation is advised in children with optimal renal transplant function and a patent elbow AVF associated with lowered distal tissue perfusion.

CASE DESCRIPTION

A 14 year old girl visited our department of vascular surgery with a history of progressive pain and cramps in the left hand and a painful dilatation of the AVF. She had developed progressive kidney failure due to segmental glomerulosclerosis from her fourth year on. She commenced hemodialysis on the age of 8 using a brachio-cephalic elbow AVF in her left arm (figure 1). After 8 months of hemodialysis, diminishing access flows required Duplex evaluation and a stenosis of the proximal left brachial artery was diagnosed. Surprisingly, the radial artery originated just distally of this stenosed segment halfway the upper arm. Moreover, the radial artery in the lower arm demonstrated retrograde flow (towards the elbow). A normal subclavian and axillary artery as well as a patent venous outflow tract were found after Seldinger angiography. As a sudden AVF occlusion was feared, a percutanous transluminal angioplasty (PTA) of this 4 cm brachial artery stenosis was attempted twice but to no avail (figure 2). At the age of 9, while waiting for an alternative right elbow AVF, she underwent successful kidney transplantation. The patent left arm AVF was not ligated as it did not bother her.
Five years later she visited our department of vascular surgery because of progressive complaints of her left arm and hand. Physical examination demonstrated an aneurys-

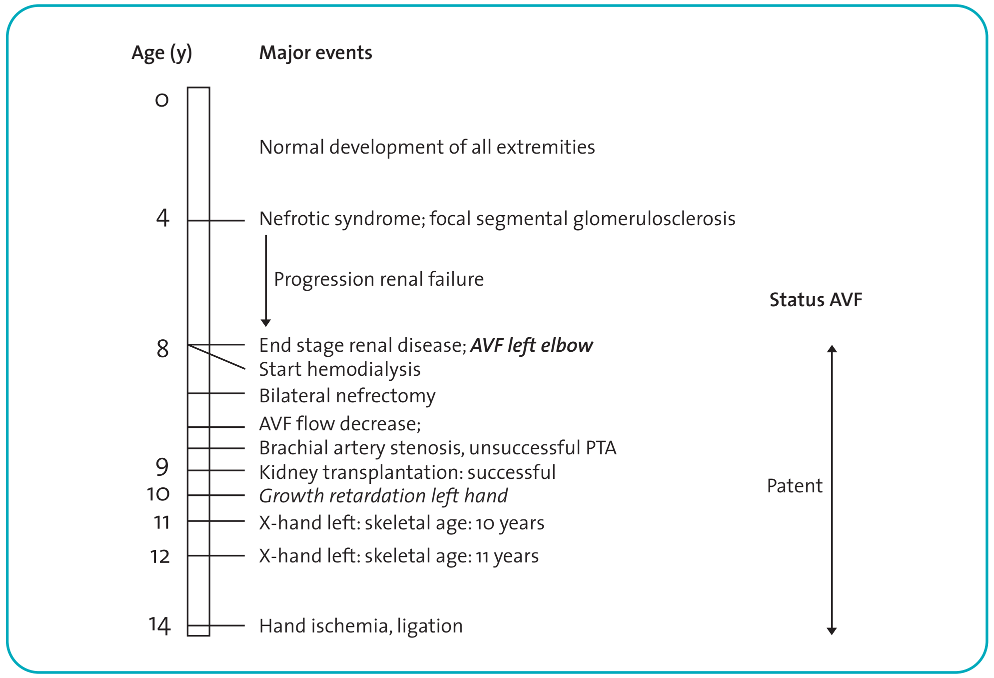

Figure 1 Schematic representation of major clinical events in study patient.

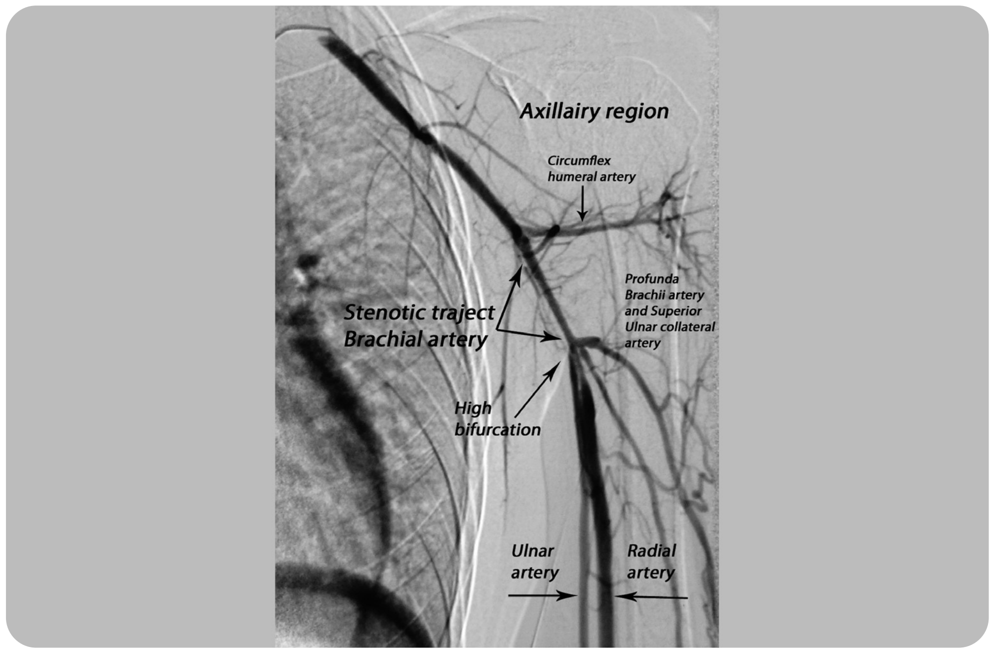

Figure 2 Seldinger angiogram demonstrated an uncommonly high origin of the radial artery at the level of the upper arm. The present figure represents a stenotic segment of the brachial artery.

matic AVF with an intense thrill. The left hand was significantly smaller compared to the right hand and appeared ischemic (figure 3). Pulsations of the left radial artery were absent but were clearly palpated on the right side. Left lower arm and hand strength were decreased, and the palm's sensibility was diminished. Duplex ultrasound identified a stable brachial arterial stenosis. Access flow was 1400 ml/min (normal: 500-800 ml). The 'ischemic score' was 87 (normal < 50) (4). HAIDI with associated delayed limb growth was diagnosed followed by an uncomplicated access ligation and physical therapy. One year postoperatively, the patient was free of ischemic symptoms (steal score, 0). The left hand was still somewhat smaller but radial artery pulsations were present. Duplex ultrasound showed a normal direction of blood flow in the radial artery (towards the hand). Systolic left radial arterial blood pressure at elbow level was 95 mm Hg compared to 119 mm Hg of the right brachial artery reflecting a persistent hemodynamically active brachial artery stenosis. Finger pressures of the right and left index finger were 115 mm Hg (digital brachial index (DBI), 0.97) and 129 mm Hg (DBI, 1.36), respectively.

Figure 3 Retarded growth of the left hand after chronic hypoperfusion due to a stenotic brachial artery and a high flow arteriovenous fistula

DISCUSSION

The long term presence of an arteriovenous fistula (AVF) in a limb usually results in augmented nutritive perfusion and accelerated tissue growth (3). Even though our patient harboured a high flow hemodialysis AVF for more than 6 years, she demonstrated retarded growth of the ipsilateral left hand. This untoward phenomenon may be explained by the presence of a stenotic brachial artery coupled with an unusual high origin of the radial artery.
Arterial stenoses or occlusions are universally found in adult hemodialysis patients and are mostly due to diabetes mellitus and progressive atherosclerosis (5,6). In contrast, stenotic arterial disease during early childhood is rare. Takayasu arteriitis is a chronic inflammatory disease that may develop during childhood and is mainly affecting aorta and its main branches. One such patient demonstrated symptoms of upper limb hypoperfusion due to a narrowed subclavian artery (7). However, most of these children develop hypertension due to renal artery occlusions. Duplex ultrasound in our patient showed patent renal arteries, whereas a bilateral angiography demonstrated normal anatomy of subclavian and axillary vasculature. Takayasu arteritis is therefore unlikely. Nevertheless, it is thought that the presence of a stenotic segment of the main artery feeding the lower arm acted as a prerequisite for growth retardation of the hand.
Also the uncommon phenomenon of a high origin radial artery in itself may not be crucial in the pathophysiology of the present hand hypoplasia. Adult upper extremity arteriograms identified major anatomic variants such as high devision of the brachial artery in 7% of individuals (8). Moreover, a study of 750 upper extremities demonstrated a 19% major arterial variation rate, most frequently regarding origin and position of the radial artery (9). Interestingly, variants of the brachial artery were predominantly (ratio 1.5:1) found on the right side compared to the left. However, these variants are not necessarily associated with a higher incidence of stenosis or ischemia of the hand.
We hypothesize that a hemodynamically important stenotic brachial artery segment combined with a high division of a radial artery feeding a high flow AVF is responsible for the retarded hand growth. If these aberrations occur simultaneously, the phenomenon of steal may happen (10).
Steal is typically observed in a clinical syndrome termed 'subclavian steal syndrome'. In these patients, reversed direction of vertebral artery blood flow due to an upstream stenosed subclavian artery leads to cerebral ischemia (11). A similar phenomenon has occurred in our patient. She demonstrated reversed blood flow in the lower arm radial artery as a result of an upstream stenosed brachial artery. A low resistance, high flow elbow AVF connected to a relatively small calibre radial artery resulted in an even more pronounced drop in blood pressure just distal to the anastomosis ('pressure sink') (12). This local phenomenon of low arterial pressure at the AVF anastomosis 'attracts' substantial amounts of blood flow, quantities that are subsequently 'stolen' from the hand

in an attempt to maintain access flow. A reversed direction of radial blood flow was indeed demonstrated using Duplex techniques. Forward flow through the ulnar artery and collaterals apparently were not able to compensate for this retrograde flow in the radial artery as persistent hand ischemia occurred. After AVF ligation, ischemic symptomatology subsided and direction of blood flow in the radial artery determined by Duplex returned to normal.It remains unclear what triggered this 14 year old adolescent to consult our department more than 5 years after access construction. Ischemia may have intensified due to increased nutritive demands following accelerated puerperal growth. An alternative explanation may just be the fact that HAIDI often takes several years to develop, especially in autogenous elbow accesses (13).

Complications associated with a persistently patent AVF ad fuel to the discussion whether an AVF requires ligation following successful renal transplantation in children. Long term complications of an AVF include high blood flow (9%) or distal ischemia (1%) (2). Persistent high access flow may result in cardiac overload and failure due to left ventricle dilatation and hypertrophy (14). Interestingly, these adaptations may appear reversible following access ligation (15). In adults, ligation is advised if access flow is above 1000 ml/min, particularly if cardiac risks are substantial and probability of renal graft loss is low (14,16). AVF ligation is even more logical in the presence of hand ischemia. We did not found recommendations in the literature on follow-up in patients after renal transplantation and persistence of an AVF. A regular control after successful renal transplantation (6 months, 1 year, yearly thereafter) may be advised including monitoring of the AVF flow and echocardiographic studies. If AVF flow exceeds 20% of the circulating volume flow or left ventricle dilatation is present, ligation of the AVF is advised (NYHA III-IV patients excluded).

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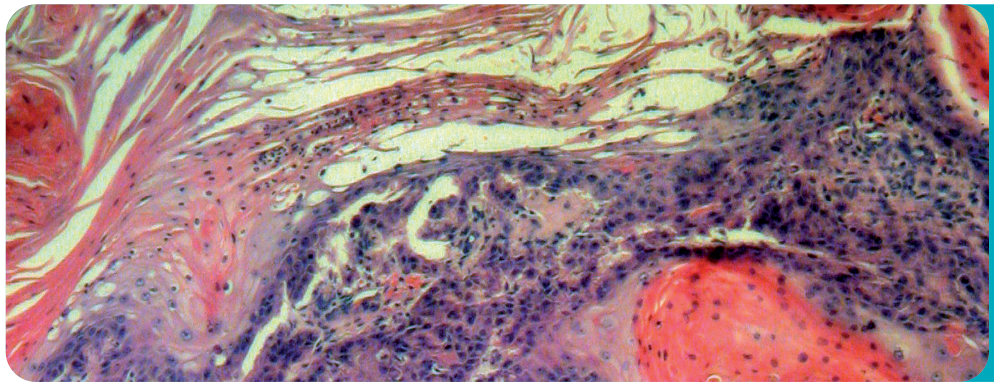
CHAPTER 9



Multiple carcinomas in a hemodialysis access induced ischemic hand of a renal transplant patient

F. van Hoek, H.W. van Tits, I. van Lijnschoten, B.D. de Haas and M.R. Scheltinga

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ABSTRACT

Long term immunosuppression following organ transplantation promotes the onset of skin cancers. A renal transplant patient developed multiple hyperkeratotic nodi in a left hand and digital pain following prolonged immunosuppression. Several skin abnormalities were observed in an ischemic and atrophic left hand in the presence of a patent Cimino-Brescia arteriovenous fistula previously used for hemodialysis. Severe hand ischemia was confirmed by digital plethysmography. Pathological examination of all 7 excised skin lesions indicated manifestations of well differentiated squamous cell carcinomas (SCC). Severe locoregional ischemia due to an intact hemodialysis access may enhance toxic effects of chronic immunosuppressive medication. Oxidative stress may act as a co-carcinogenic factor for the development of SCC in renal transplant patients receiving immunosuppressive agents.

BACKGROUND

Exposure to ultraviolet radiation (UV) is the most important cause of squamous skin cell carcinoma (SCC). However, prolonged use of immunosuppressive agents also greatly enhances a lifetime risk on SCC as a 70% incidence is noted in patients receiving immunosuppression >20 years (1). SCC is the most common skin cancer in transplant recipients, occurring up to 250 times as frequently compared to other populations (2). UV and immunosuppressive medication are thought to use similar pathways as these factors both inhibit antigen-presenting cells including Langerhans' cells (3).
Prior to renal transplantation, most patients depend on an access for hemodialysis (AVF, arteriovenous fistula). Ongoing maturation of an autogenous AVF incidently leads to locoregional hypotension and decreased distal extremity perfusion (4). Cardinal symptoms associated with 'hemodialysis access induced distal ischemia' (HAIDI) are pain, cramps, diminished sensibility and coldness of the ipsilateral hand (5). Occasionally, HAIDI may progress to severe tissue loss or even amputation (6). Therapy is aimed at restoring distal perfusion by medication or by an (endo) vascular technique (7).
A renal transplant patient develops 10 manifestations of SCC over an 18-month period, 7 of them in a severely ischemic dialysis hand. It is hypothesized that locoregional oxidative stress due to an autogenous dialysis access may accelerate the development of local SCC's in renal transplant patients receiving long term immunosuppression.

CASE REPORT

A 47-year old male patient visited our dermatological department in 2007 with several skin abnormalities on the head and left upper extremity combined with pain in all fingers of his left hand. He had received kidney transplants in 1979 (rejected some years later) and in 1987. He was a chess player by profession, refrained from smoking and avoided sun rays. As his current kidney function was suboptimal (GFR 27 ml/min), his AVF (autogenous radiocephalic, 'Cimino-Brescia') was to remain patent for possible future use. He had received 175 mg of azathioprin and 10 mg of prednisolon once daily for more than 25 years. Three hyperkeratotic lesions (two on head, one on dorsum left hand) were removed under local anesthesia. Healing of the incision on the left hand occurred with delay including slow development of granulation tissue. Pathological examination revealed 3 well differentiated squamous cell carcinomas. Additional blood testing on HIV and HPV was negative. In the following year he developed 7 additional manifestations of SCC, 5 again in the left lower arm and hand region, and 2 on the forehead. A large SCC located on the ulnar side of the left hand required resection of the fifth metacarpal bone. Wound healing was again delayed. Pathological examination of all 7 SCC's harvested from the lower arm and hand revealed well differentiated carcinomas.

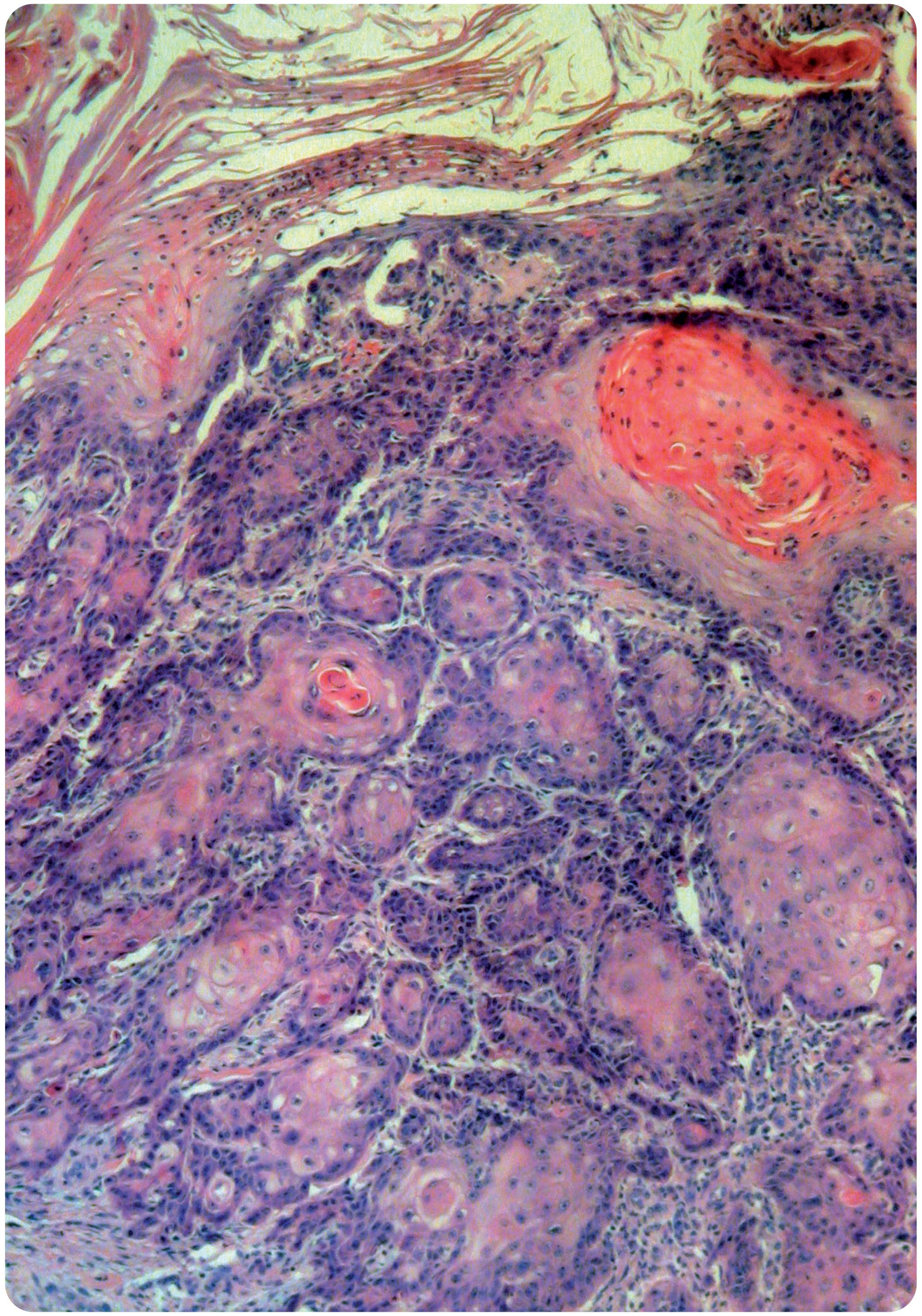

Figure 1 Squamous cell carcinoma of the left lower arm. Infiltratively growing tumor originating from the epidermal layer containing capriciously formed groups of atypical squamous epithelia (Magnification 50x, HE coloured).

Neoangiogenesis was observed but perineural invasion was absent (figure 1). Staging for exclusion of metastases was not performed. He presented to the department of vascular surgery in 2008 as the left hand pain was progressive. Examination of the left hand revealed atrophy and an intense coldness suggesting ischemia (figure 2). A thrill was palpated over a well matured Cimino-Brescia AVF. Radial arterial pulses were absent and capillary refill was slow. In contrast, the right hand was well perfused. His ischemic score was 184 indicating severe ischemia. Ischemic scores in a normal dialysis population range from 30-50 (5). However, patients requiring surgery for HAIDI demonstrate mean scores of 153±33 (7). AVF flow determined using a time transit method was 2000 ml/min (normal: 300-600). Photoplethysmographic measurements demonstrated an immeasurably low digital pressure (0 mm Hg) indicating hemodialysis access induced distal ischemia (HAIDI). In contrast, right digital pressures were normal (>120 mm Hg). Seldinger angiography excluded an arterial stenosis. However, the hand itself was poorly perfused. It was decided to perform a surgical exploration aimed at lowering access flow ('banding') as this manoeuvre enhances digital perfusion pressures (8). Intraoperative AVF clamping nihilated access flow but finger pressures remained untracably low. Banding was aborted but a conservative treatment including attenuation of antihypertensive medication resulted in higher systolic pressures and subjectively diminished pain. He died in October 2008 as a result of complications following a cardiovascular operation.

Figure 2 Several hyperkeratotic nodi in the severely ischemic hand. The patient required fifth metacarpal resection because of penetrating squamous cell carcinoma.

DISCUSSION

Risk factors for SCC include UVB light, smoking, aging, p53 gen polymorphism or glutathione peroxydase inhibition (3,9). Longterm exposure to immunosuppressive medication (azaothioprin in particular) dramatically increases the risk of SCC in transplant patients (10). The type of immunosuppressive medication administered after chronic UVB light exposure also appears very relevant for number and size of skin tumors as cyclosprin-A treated mice showed larger tumors with a higher rate of malignancies compared to controls (11).

The presence of 10 SCC's in a renal transplant patient is not unique after almost three decades of immunosuppression. However, all 7 hand SCC's occurred in the ischemic hand and not one in the other, well perfused hand. This difference was not explained by differential sun exposure as our patient avoided sun rays. However, this finding suggests chronic ischemia as a possible co-carcinogenic factor.

There is evidence to support the contention that chronic hypoxia may stimulate carcinogenesis on a cellular and on tissue level. A hypoxic cellular environment may develop in cancer tissue during uncontrolled multiplication, and malignant cells are found to develop strategies for survival under these unfavourable circumstances. For instance, cells may activate substances such as SENP1 that may help malignant cells to even thrive under hypoxic conditions (12). Other studies have suggested a role for reactive oxygen substances in the promotion of skin malignancy (13). A hypoxic skin microenvironment contributed to transformation of melanocytes indicating that lack of oxygen may serve as a tumor promoting stimulus for dermal cells (14). Moreover, chronic hypoxia was found to exert carcinogenic effects in liver tissue as reflected by accelerated outgrowth of colorectal micrometastases in an animal model (15).

Biochemical evidence also supports the hypothesis of hypoxia-induced carcinogenesis. For instance, the transcription factor Hypoxia-inducible Factor 1 (HIF-1) plays an important role during cancer progression by transactivating multiple genes which regulate microvasculature, glycolysis, oxidative phosphorylation, cell motility, migration, tissue invasion and metastasis. HIF-1 is essential for O_2 regulation in two ways. During hypoxia it can increase O_2 availability by transactivating a gene pathway. On the other hand, it regulates diminished metabolic function. Under selected circumstances HIF-1 acts as a tumor suppressor gene by up-regulating two other genes (Ndrg1 and Selenbp1). The expressions of those two upregulated genes are lost in human epithelial malignancies and are associated with a poor prognosis (16).

But there is more biochemical evidence. Urinary 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG), a marker of oxidative stress, was elevated in renal transplant patients with SCC compared to those without (17). Interestingly, exposure to azaothioprine was positively associated with levels of 8-oxodG. A subpopulation of renal transplant patients apparently is under greater oxidative burden, and this group is particularly predisposed to skin cancers. Markers of oxidative stress including HIF-1 were not measured in our patient.

Are there any clinical data suggesting carcinogenesis following chronic hypoxia in transplant patients? In a subgroup of renal transplantation patients with an AVF, upper limb skin cancers were more prone on the AVF arm than on the other side. After examining that whole population however, no significant relation was found between an AVF and upper limb skin malignancies (18). As AVF access flow and finger pressures were not measured, it is unclear if digital perfusion was diminished in this subgroup of skin cancer-prone patients.

Our patient acted as a bizarre experiment in itself as his contralateral, normally perfused hand served as a control and remained devoid of SCC's. If the outbreak of SCC's in his ischemic hand were due to a sustained direct local carcinogenic effect of immunosuppressive agents, one would expect a lower incidence in a severely hypoperfused limb. In contrast, multiple SCC's developed in the ischemic hand, and thus progressive hypoxia may have superseded immunosuppression as a dominant risk factor.

Therapeutic strategies may focus on attenuation of the locoregional ischemic state. Several techniques for treatment of HAIDI have been promoted including endovascular manipulation (e.g deblocking inflow stenosis), or vascular surgery. Hand ischemia in the presence of a high flow hemodialysis facility (>2000 ml/min) is effectively treated with banding guided by monitoring of access flow and digital pressures (7). If however a renal transplant functions well, one may consider AVF ligation. Future studies may elucidate whether the augmented risk on skin malignancies associated with a greater hypoxic burden is diminished after attenuating systemic levels of oxidative stress.

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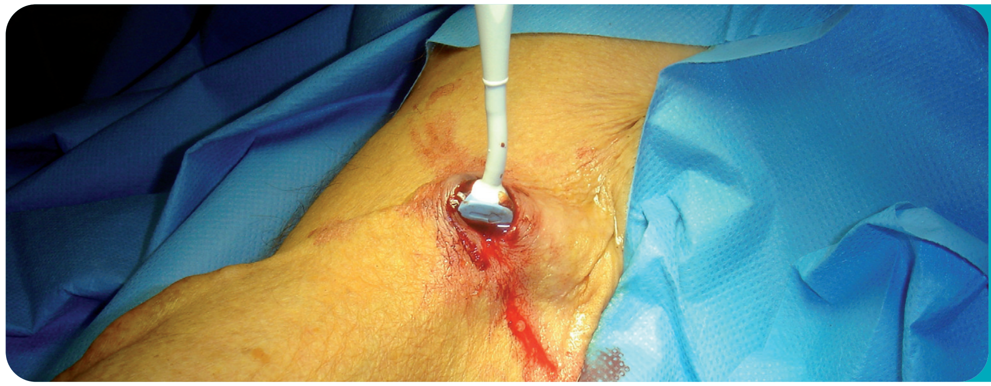
CHAPTER 10



Banding for high flow hemodialysis access

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INTRODUCTION

The number of autogenous brachio-cephalic upper arm direct access is expected to rise in the coming decades at the expense of radio-cephalic access. Although the longevity of these upper arm dialysis facilities is optimal, a small portion leads to complications including distal ischemia (HAIDI, hemodialysis access induced distal ischemia) and/or inappropriate high flow (> 2 l/min).
A high flow access (HFA) usually allows effective hemodialysis but may exhaust cardiac capacity over time. One may hypothesize that a HFA contributes to unexplained high mortality rates in a dialysis population. Therefore, attenuation of high flow in a dialysis access may protect cardiac function and prove beneficial for long term patient survival. Aim of this overview is to discuss several aspects of HFA and to evaluate a surgical technique termed banding.

BACKGROUND

Cardiomegaly and congestive heart failure due to abnormal arteriovenous connections have been identified as early as the 1950's (1). A 1967 report critically evaluating patients with a radio-cephalic direct wrist access (Cimino-Brescia fistula) suggested adverse effects on cardiovascular performance (2). It was initially questioned if changes in cardiac function were temporary or not. Some years later, cardiac failure due to a HFA appeared reversible. A high flow wrist access in a patient with an cardiac output >11 l/min underwent correction by application of a clip close to the arteriovenous anastomosis. The patient subsequently mobilized generalized edema and recovered from cardiac decompensation (3).
Incidence of HFA and associated cardiac failure is unknown but depends on definition, index of suspicion, and preferences of the multidisciplinary dialysis team. One study found a 3.7% (17/460) incidence of HFA requiring surgical correction (4). Another study, reporting on effects of operative banding of HFA, found a 1 to 5 ratio for cardiac overload (n=17) and HAIDI (n=78), respectively (5). In contrast, a small pilot study (n=16) demonstrated an equal distribution between these complications (6). As about 5% of a regular dialysis population receives surgery for HAIDI, one may assume that a slightly smaller fraction of patients (2-4%) may harbour HFA requiring correction. Incidence of HFA associated with cardiac overload requiring surgical intervention is expected to rise as more dialysis centers will adopt a regimen of regular interval flow measurements as suggested by DOQI.

Pathophysiology of cardiac overload due to HFA

Construction of an autogenous direct access for dialysis leads to an immediate 10-20%

increase in cardiac output due to lowered peripheral vascular resistance and increased sympathetic nervous system activity. Both augmented blood volumes and higher levels of natriuretic peptides are observed in the weeks following access construction (7). If some hitherto unidentified trigger (gradually enlarging anastomotic area, progressive loss of venous tone, ongoing hormonal or sympathetic stimulation, 'positive remodelling') precludes attainment of a steady state, chronic systemic overload and left ventricular hypertrophy may occur. As a consequence, decompensation may ensue resulting in progressive cardiac failure and death.

Fortunately, this chain of events leading to cardiac overload may be reversed. For instance, regression of ventricular hypertrophy is observed following HFA closure in patients harbouring a well functioning kidney transplant (8,9). These data strongly suggest that cardiac phenomena associated with a HFA are, to some extend, reversible.

Patient's history and physical examination

Once cardiac reserve fails in the presence of a HFA, a previously asymptomatic patient may experience increased body weight, fatigue and shortness of breath during minimal exertion or rest. Physical examination reveals classical signs of cardiac decompensation including dyspnoea, tachypnoea and peripheral edema as well as systolic bruits or a gallop rhythm.

Inspection of the dialysis access may demonstrate grossly dilated arm veins in the presence of a direct radiocephalic access (figure 1) or a brachiocephalic access (figure 2). An intense thrill is usually palpated, and radial artery pulsations may be diminished or absent possibly indicating accompanying digital ischemia. The association of high flow and distal ischemia is frequently observed.

The clinical significance of a positive 'Nicoladoni-Branham' sign is unclear. This reflex may occasionally be elicited after manual compression of the HFA. After access occlusion, increased systemic blood pressure will stimulate aortic and carotid baroreceptors leading to vagal stimulation and subsequent bradycardia. A positive test may not always predict successful HFA correction or reversibility of cardiac failure, and sensitivity and specificity may be low (3,10). An older study found that this sign was only present in 1 of 13 patients with a HFA (11). In contrast, a recent study reported that all patients (n=15) who had undergone successful HFA correction (70% drop in access flow) associated with a 2.4 L drop in cardiac output had demonstrated a positive test preoperatively as reflected by a reduced pulse rate of at least 20% (4). It is hypothesized that a positive Nicoladoni-Branham sign is associated with young age, degree and time of exposure to cardiac overload, and capacity of cardiovascular adaptation. For instance, a 27-year young athlete with a 19.4 l/min cardiac output demonstrated a 25 beat drop in heart rate (12). In a clinical situation, a positive sign may support a decision to embark on corrective surgery.

Figure 1 Inspection of a high flow dialysis access may demonstrate grossly dilated lower arm veins.

Figure 2 A high flow dialysis access of the upper arm.

Risk factors for HFA and cardiac overload

It is largely unknown which factors contribute to the development of high flow once a hemodialysis access is created. A prosthetic lower- or upper arm loop or straight graft may harbour a certain risk immediately after implantation but not later on. In contrast, an autogenous brachio-cephalic upper arm direct access matures and may enlarge substantially over the years. In general, chronic HFA predominantly occurs in an autogenous upper arm access (4-6,13).

If a dialysis patient is relatively young, fit and non-smoking, intact adaptive mechanisms may facilitate ongoing maturation of an access. The arterial tree as well as venous outflow tract accomodating an autogenous brachio-cephalic upper arm direct access may gradually demonstrate positive remodelling (figures 3,4). These exhibitions of hypertrophy may take several years to develop. A comparison between groups of patients requiring operative correction for a HFA or for HAIDI indicates that the HFA group was 4 times longer on dialysis (HFA: 87±19 months vs HAIDI 23±6 months) (14). Onset and incidence of high flow is also determined by the access' location (upper > lower arm) and type of anastomosis (large > small, side-to-side > end-to-side) (15).

Patient risk factors for the development of cardiac failure in the presence of a HFA include long term hypertension and coronary artery disease. These conditions already may have restricted cardiac capacity and pose a risk for cardiac failure in the presence of a dialysis access (8). These premorbid patients will experience symptoms associated with increasing access flows in an earlier stage compared to relatively healthy individuals. Interestingly, and in contrast to HAIDI, diabetes mellitus is not associated with HFA supporting the supposition that development of a HFA requires relatively intact adaptive sympathetic mechanisms.

Diagnostic modalities for HFA and cardiac overload

High flow is detected during routine measurements of access flow using standard techniques. DOQI advises to monitor flow every two months using a two-needle dilution approach (Transonic Systems Inc, New York, USA). Other studies reported on access flow monitored by alternative techniques including electromagnetic probes (16), ultrasonic transit time methods (6) or transcutaneous Duplex measurements (8).

Once a HFA is diagnosed and deemed associated with cardiac overload, an electrocardiogram may demonstrate cardiac strain including signs of hypertrophy. Echocardiography is used to confirm an increased left ventricular mass index and high end-diastolic diameters and excludes additional coexisting pathology (9). Optional cardiac catheterization diagnoses increased cardiac output in the presence of low peripheral vascular resistance. Moreover, oxygen handling is disturbed as reflected by both low arterio venous differences and low extraction rates (6,9). Conversely, temporary or permanent occlusion of a high flow access reverses these abnormalities towards near normal levels (8,17). Clear cut criteria for treatment of HFA in the presence of cardiac failure have not been

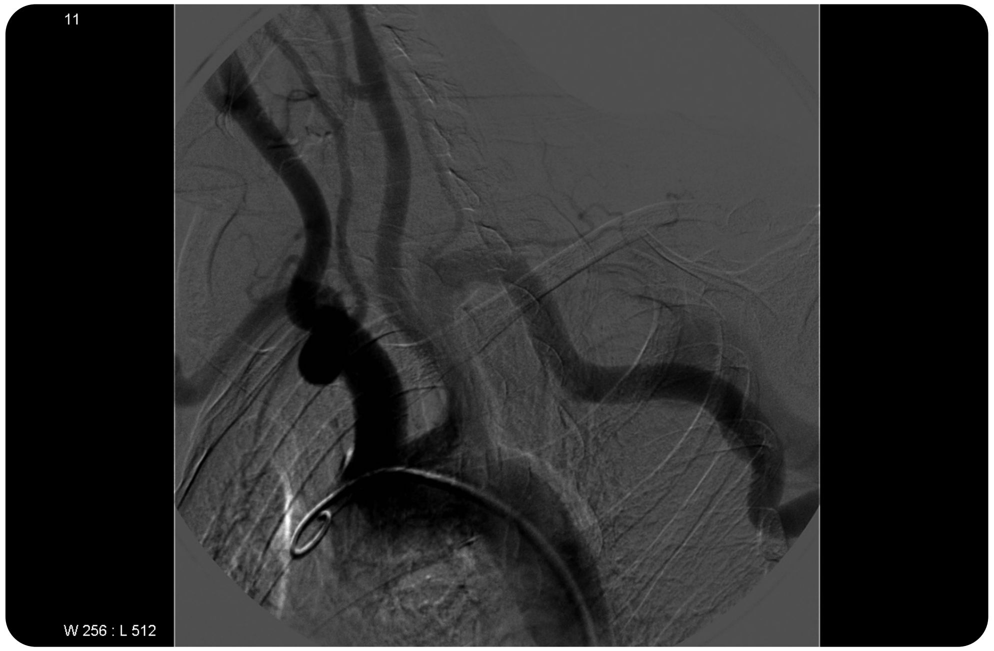

Figure 3 Seldinger angiography of the proximal tree accommodating a high flow upper arm dialysis access. Note the difference in diameter between the subclavian artery feeding the access (left) compared to the other side.

Figure 4 Same patient as in figure 3. Both brachial artery and vein demonstrate substantial hypertrophic dilatation, particularly striking when compared to a normal sized humeral bone.

established. Some used access flow threshold levels ranging from 1.2 to 2.0 L/min (4-6), whereas others suggested to rely on an increased cardiac index (> 3 L /min.m2). A two-liter access flow cut-off point predicted cardiac insufficiency in a recent study (13). A decision to treat HFA and concomitant cardiac overload should also depend on additional comorbidity and life expectancy.

Non-surgical management of HFA

The first line of treatment for patients with cardiac insufficiency and a HFA is nonsurgical. Usual causes for cardiac overload including anemia, electrolyte imbalances and hypertension need correction by a nefrologist. A cardiologist may modify cardiac medication possibly guided by echocardiographic results. Surgical correction of a HFA is indicated if conservative treatment fail.

Vascular surgery for HFA

Several surgical techniques have been proposed for invasive management of a HFA in the presence of cardiac overload. All methods aim at reducing access flow with maintenance of an adequate dialysis access.

Access flow theoretically may be reduced by increasing the resistance of the arterial inflow, by increasing the resistance of the anastomosis, or by increasing the resistance of the efferent vein(s)(31).

Reducing the diameter of the arteriovenous anastomosis should limit the high access flow. However, surgically reducing the anastomic diameter is challenging and technically demanding as objective parameters reflecting access flow are scarce. One study in 18 patients reported on results of narrowing the arteriovenous anastomosis. Diameters of autogenous access facilities were reduced from 7 to 4 mm resulting in a 2 L/min reduction of access flow as monitored by intraoperative Doppler ultrasonography. Moreover, cardiac output was lowered from 8.5 to 6.1 L/min (18).

Alternatively, one may disconnect the anastomosis and construct a novel one with a smaller diameter on the same location, using a small piece of interposition graft (19). A prosthetic graft may also be inserted between an other, smaller capacity artery and the venous system. This latter option was found to lead to a 50% to 70% reduction in access flow whereas cardiac output decreased by 30% (4,20).

The oldest technique for treatment of HFA and associated cardiac failure is banding. This surgical approach is introduced in the early 1970's and is based on narrowing the access' venous outflow tract (16). The arterio venous anastomosis itself remains unaltered but an iatrogenic stenosis is introduced around the access' venous leg. The vein diameter is reduced by stitches, plication or by partial wall resection. Future dilatation is prevented by wrapping a 0.5-1.0 cm wide Dacron of Teflon band around this piece of modified vein ('banding'). Several stitches may fix the band once the desired grade of constriction is attained (21). Although results of banding for HFA were encouraging

(16,21), dismal access patency rates after banding for treatment of HAIDI may have tempered enthousiasm for the technique (22).

Success rates of banding in general entirely depend on the use of intraoperative monitoring tools guiding grade of the band's constriction. A banding technique is only clinically effective for HFA if access flow is measured simultaneously during the operative procedure (figures 5-7). Early banding proponents advised the intraoperative use of electromagnetic flow probes for monitoring access flow (16,21). Interestingly, manipulating access flow in a HFA greatly influenced finger pressures as well as central venous saturation indicating their interrelationship (6). Conversely, monitoring these parameters during a banding procedure may help the surgeon to determine grade of constriction. Specifics of studies on efficacy of banding in patients with HFA and cardiac insufficiency are depicted in the table (5,16,21,23-26). Most patients harbour an autogenous upper arm access. Mean flow decreased from 2.1±0.4 L/min to 0.8±0.2 L/min following surgical banding. The majority of patients (95%, 42/44) improved in the postoperative period as reflected by attenuated symptoms and lessened signs of cardiac insufficiency.

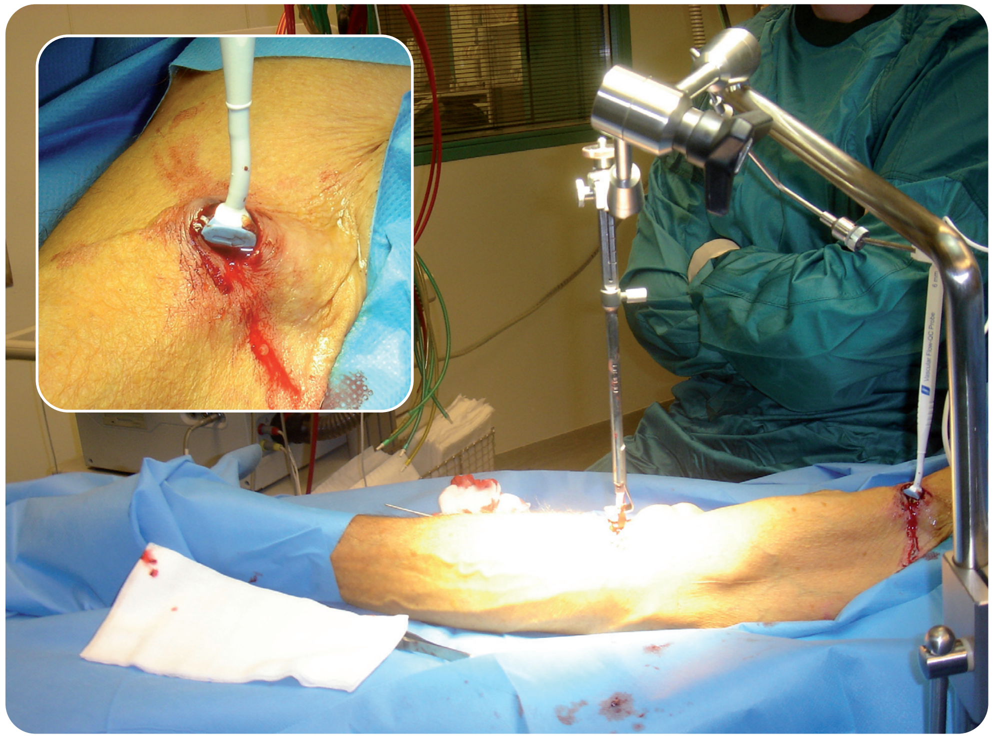

Figure 5a Banding of an access for HFA is performed using intraoperative flow control as the remaining flow should always exceed thrombotic threshold levels. Flow is measured using transit time technology. If a patient suffers from a combination of HFA and digital ischemia (HAIDI), digital pressures are simultaneously monitored using photoplethysmography.
Figure 5b Close up of flow probe measuring access flow continuously.

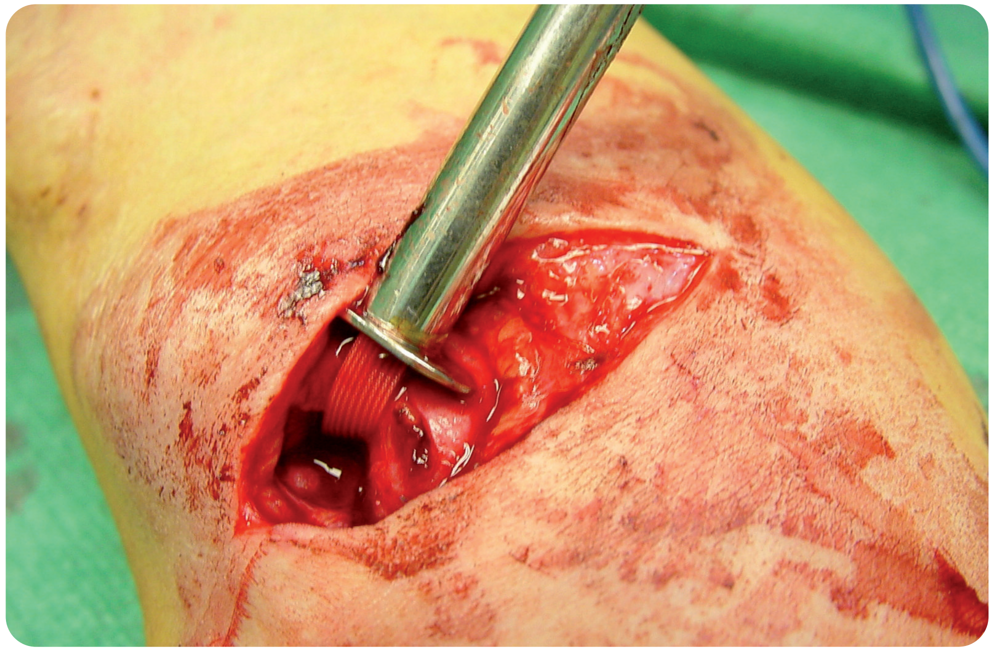

Figure 6 *Intraoperative view of a band encircling the venous portion of a HFA. Grade of constriction is determined by readings of access flow (in case of HFA only), or by alterations of flow and finger pressures (HFA combined with HAIDI).*

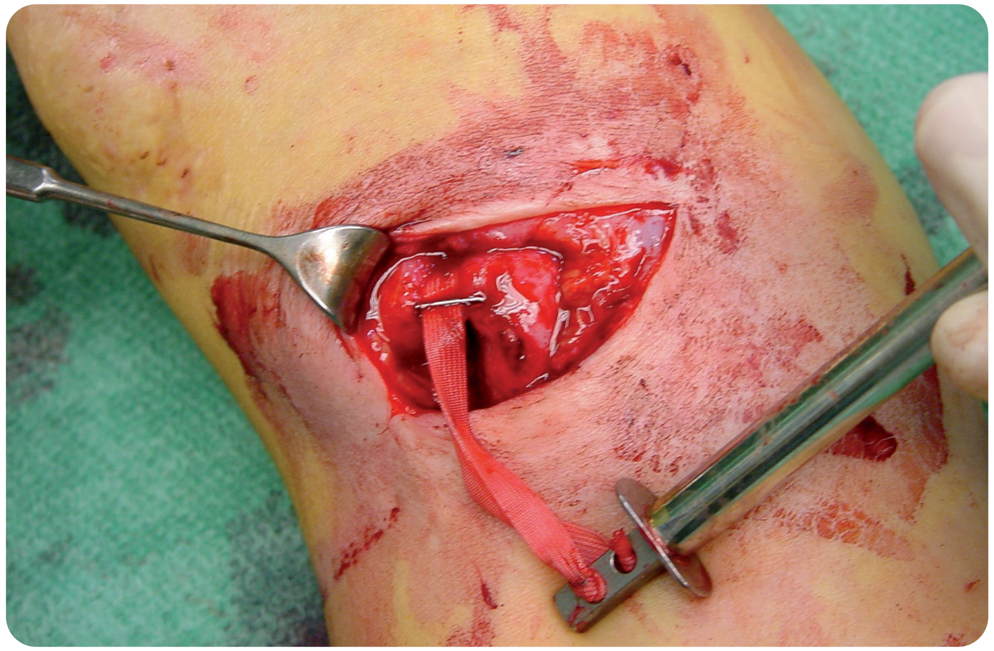

Figure 7 *Once the desired level of access flow and finger pressures is obtained, the band's constriction level is secured by a clip and stitches.*

Author	Year	Ref.	Number of patients	Age	Access location	NB sign	Months on dialysis	Flow preop	Flow postop	Intraoperative tool	Symptoms/signs	Follow up (months)	Complications
De Palma	1973	16	1	60	Leg	+	nr	2.5	0.6	EM probe	Improved	nr	-
Anderson	1975	21	3	45 48 51	Wrist Wrist Wrist	- - -	48 30 30	2.1 1.4 2.9	0.5 0.7 0.6	EM probe EM probe EM probe	Improved Improved Improved	8 7 9	- - -
Isoda	1994	23	1	49	Wrist	nr	24	3.7	1.4	EM probe	Improved	42	-
Tzanakis	1999	24	1	48	Wrist	nr	nr	1.6	0.5	'Blind'	Improved	6	-
Murray	2004	25	1	55	Elbow	nr	52	5.2	2.9	Intravenous catheter	Improved	12	-
Zanow	2006	5	17	59±3	Elbow > wrist	+	72% > 12 months	2.1±0.5	0.5±0.7	EM probe/ transit time technique	96% improved	6-37	-
Schneider	2006	26	20	62±3	Elbow > wrist	nr	nr	2.0±0.5	1.0±0.2	"Blind"	95% improved	1-3	20% occlusion/ hematoma
Total			44										
Mean				59±3				2.1±0.4	0.8±0.2			11±3	

Table ***Studies reporting on clinical success of banding of high flow access associated with cardiac overload.*** *nr: not reported; NB sign: Nicoladoni-Branham; EM probe: electromagnetic; blind: banding without monitoring access flow or digital perfusion*

DISCUSSION

The present overview demonstrates that patients with a high flow dialysis access and cardiac overload benefit from surgical banding. A simple management scheme is proposed (27). Each dialysis patient routinely undergoes measurements of access flow according to the DOQI recommendations. Cardiological evaluation using echocardiography is indicated once high flow (> 2l/min) is repetitively observed. Non-surgical management including correction of hypertension, anemia, and electrolyte disturbances is intensified. Once signs of cardiac overload persist under optimal medical management, the multidisciplinary team including a nefrologist, a cardiologist and a vascular surgeon may decide to initialize invasive evaluation aimed at surgical HFA correction. Concomitant symptoms and signs of distal ischemia (HAIDI, hemodialysis access induced distal ischemia) (14) as well as a positive Nicoladoni-Branham sign may support this decision. The access anastomosis and venous outflow tract including sidebranches are visualized using Seldinger or magnetic resonance angiography, or Duplex.
Based on these findings and the patient's general condition, the team may decide to offer surgical correction. Surgery can be performed using general anesthesia but is ideally carried out using a locoregional technique in day care. Intraoperative monitoring of access flow and digital perfusion is mandatory. Ligation of large sidebranches (basilic vein) may lead to a profound decrease of access flow while associated digital ischemia is attenuated as reflected by an increase in digital-brachial index. One may decide to terminate the surgical procedure at this point. However, if sidebranch ligation does not result in a substantially diminished access flow, or sidebranches are absent while most of the flow is shunted towards the axilla by a single route (cephalic vein), the surgeon may decide to perform banding. Again, constriction of the band is guided by alterations in access flow and digital pressures. Timing of corrective surgery is controversial. It may well be that the window of opportunity for invasive treatment is restricted. Once cardiac reserve is depleted following prolonged systemic overload, myocardial damage may have become irreversible.
Management of a patent dialysis access following successful kidney transplantation is a matter of debate. Some advice ligation (10) whereas others are reluctant to do so as access closure may lead to an intense hypertension and increased requirements of antihypertensive medication (12). Data supporting access ligation in patients with optimal kidney and cardiac function are absent. However, one may advice ligation in case of HFA, left ventricular dilatation, high risk for cardiac events or low probability of transplant loss (28).
Complications including infection, mycotic bleeding or aneurysms following banding for HFA were not found in the literature. Interestingly, banding does not result in accelerated venous intimal-medial hyperplasia (29). Immediate postbanding access occlusion is seldomly reported in patients operated for HFA as depicted in the table (4%, 2/44).

Strikingly, the only two patients whose banded access appeared occluded were operated without the guidance of intraoperative flow monitoring ('Blind' banding, table) (26). High rates of clinical success and low incidence of access occlusion associated with banding for HFA may seem to contrast with clinical data following banding for HAIDI. The apparent discrepancy is explained in several ways. Firstly, the present overview demonstrates that banding for HFA is almost always performed using intraoperative flow control. In contrast, several studies on banding for HAIDI failed to monitor access flow (22). As a consequence, bands may have been pulled too tight pushing access flow below its thrombotic treshhold (< 400 ml/min). Secondly, flow in a HFA is usually considerably larger compared to flows in an access causing HAIDI. Therefore, even after a substantial decrease in access flow following banding for HFA, residual flow may remain well above thrombotic levels. These findings again imperatively illustrate that banding for HFA or HAIDI should always be performed under flow control, ideally combined with a technique reflecting digital perfusion (e.g. photoplethysmography) (6).
The present overview indicates that high flow in an autogenous brachio-cephalic upper arm direct access is associated with increased morbidity and possibly mortality. Which surgical tricks may prevent development of a HFA following routine access construction? Randomized controlled trials are not available. Size of arteriovenous anastomosis is a major determinant. Some authors used a relatively small inflow artery feeding an upper arm access and did not observe high flow although the observation period was short (30). An intuitive surgical step is to limit the arteriotomy for a brachiocephalic or a radiocephalic direct access to a maximum of 5 mm and 8 mm, respectively.

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CHAPTER 11

Summarizing discussion, conclusions and future perspectives

GENERAL ISSUES ON HAIDI

Symptoms associated with HAIDI are diverse. In its acute form (< 24 h postoperatively), a patient experiences an intense pain in the hand, sensory losses and paralysis immediately after routine arteriovenous fistula (AVF) creation necessitating immediate surgical reintervention as tissue viability is severely compromised (1,2).
A separate acute syndrome may exclusively occur in diabetic patients with neuropathy and peripheral arteriopathy following a brachial artery AVF. Within hours after access creation, progressive muscular weakness of the hand and forearm combined with sensory loss and dysesthesia may develop (2,3). The syndrome is caused by ischemia of nerves in the elbow region and is termed ischemic monomelic neuropathy (IMN) (4). Remarkably, ischemic signs and symptoms of hand and fingers are mild or even absent (5). Early recognition and treatment of this 'proximal' ischemia may reverse these neuropathophysiological sequelae (2), but permanent neurological damage is not unusual (5). The decision to create an AVF with an anastomosis to the brachial artery should not be taken lightly in diabetic patients with manifest neuropathy and arteriopathy. If such an access is unavoidable, postoperative serial nerve conduction studies may prove helpful in predicting IMN (1,6).
The differential diagnosis of chronic HAIDI (> 1 month postoperatively) is diverse. Bone pain due to hyperparathyroidism may mimic ischemic rest pain or neuropathic hand pain. Moreover, HAIDI patients may also experience neurological symptoms associated with neuropathy due to uremia, diabetes or carpal tunnel syndrome (CTS). The likelihood of developing CTS, remarkably more frequently present in the contralateral arm (7), is related to time on dialysis (8). Symptoms are tingling sensations in all fingers, at night and during hemodialysis, Early median nerve decompression improves functional recovery (7).
In an average dialysis population, most HAIDI patients gradually develop distal ischemia over time ('chronic' HAIDI). Patients experience arm claudication or pain during dialysis (9), and later on even in resting conditions (10). Chronic HAIDI is caused by a combination of increased access flows (11) and progressive arterial atherosclerosis proximal and distal to the AVF (12,13). Uremia (14), recurrent hypotensive periods after dialysis (15) and aging likely add to the development of ischemia.
The incidence of (severe) HAIDI requiring (surgical) correction in a general hemodialysis population is estimated to approximate 5%. However, the relative frequency of symptoms associated with mild to moderate HAIDI in a general hemodialysis population is largely unknown (15). An extensive literature study reported in **chapter 2** demonstrates that subjective HAIDI symptoms include coldness of the fingers, pain, cramps, diminished sensibility and strength of the AVF hand. An 'ischemic questionnaire' was composed based on this literature study. This tool was used to qualify and quantify ischemic symptoms in a large patient population (n=120). Frequency and severity of these symptoms

were tabulated in three different AVF populations (brachio-cephalic (BC), forearm loop, or radio-cephalic (RC)). The results indicate that the incidence of each ischemic symptom was highest in the BC-group followed by the loop- and radio-cephalic-group (RC). An impressive 50% of all patients in the BC-group suffers from some form of coldness of the hand and fingers of the access side. Moreover, 79% in the BC group experiences at least one of the five ischemic symptoms. The incidence of these symptoms associated with HAIDI are much higher than previously thought.

Although a substantial portion of patients apparently suffers from mild or moderate HAIDI, the occurrence of severe HAIDI is low. However, it is unclear how or when a mild patient proceeds to develop the severe form. A relation between severity and frequency of HAIDI symptoms and access flow levels was not found in the present study population. Nevertheless, in clinical practice it is advisable to evaluate each hemodialysis patient at regular intervals for (progressive) HAIDI.

Which signs may alert the nursing or medical staff ? Hand inspection may reveal pallor, cyanosis or skin mottling, coolness, wounds, muscle atrophy or other consequences of chronic ischemia (16). These signs (or a portion thereof) typically disappear once the access' venous outflow is manually compressed for a few seconds (17). Measuring systolic upper arm blood pressure with an occlusion cuff will impede the fistula's flow. As a consequence, a falsely high pressure may be measured when compared to an unblocked access flow. If, nevertheless, pressures are >20 mm Hg lower in the dialysis arm, a hemodynamically significant subclavian artery stenosis is probable. Interestingly, absence of such pressure differences does not preclude a hemodynamically important stenosis, as even narrowings <50% can have profound effects on distal perfusion pressures in high flow systems (18). Therefore, magnetic resonance or seldinger angiographies are of paramount importance in establishing the cause of HAIDI (15,19).

Some techniques may contribute to the diagnosis 'chronic HAIDI'. Systolic pressures are measured by an occlusion cuff distal to the AVF, i.e. around the lower arm (1) or fingers (15,20). A low systolic pressure index (SPI, forearm systolic pressure in access arm divided by contralateral arm pressure) was associated with abnormal nerve conduction in the access arm but clear cut-off points for critical ischemia were not observed (1). A digital brachial index (DBI) is obtained by dividing the systolic finger pressure by the systolic pressure measured in the contralateral upper arm. A DBI <0.6 during routine access surgery was claimed to identify patients at risk for HAIDI but positive predictive values were only 18% (21). A DBI < 0.4 in an access arm was associated with severe HAIDI although positive predictive values were low again (22). A mean DBI of 0.6 ± 0.3 (range 0.44 -1.08) that was found in our patient group also indicates that ischemia may be observed in the presence of a normal DBI (**Chapter 2**). It may be concluded that values of DBI are of relative importance for the diagnosis of HAIDI.

Which other techniques may help to establish the diagnosis of HAIDI ? Pulsatile energy of arterial flow is assessed by digital photoplethysmography (PPG) or pulse volume recording (PVR), flattened waveforms being indicative of ischemia (12,15,17,23). Abnormally low values of oxygen saturation (<80% and beyond) determined by digital pulse oximetry were found in severe chronic HAIDI (24,25). In contrast, low values of oxygen saturation in our population were not found, presumably because of the absence of patients with severe HAIDI. Physical examination of the access arm in our group of mild to moderate HAIDI generally demonstrated diminished radial artery pulsations and lower skin temperature of the hand, both subjectively and objectively. Finger pressures measured by photoplethysmography were substantially lower on the AVF side (106±33 mmHg) and returned to normal during AVF compression (154±25 mmHg, contralateral arm:155±20 mmHg). All these parameters return towards normal when the access outflow is properly blocked by manual compression while making sure that the arterial inflow is not compromised. Access compression is the most important diagnostic criterion for HAIDI and also allows for prediction of efficacy of future corrective surgery. Duplex ultrasonography may be used in HAIDI to detect arterial inflow stenoses, too large arteriovenous anastomoses and obstructive lesions in forearm, palmar arc and digital arteries, all factors that contribute to HAIDI. Seldinger or magnetic resonance angiography may identify embolic disease as a rare cause of HAIDI (26) or may visualize widespread obstructive lesions in distal arteries as substantial or sole contributors to HAIDI. Furthermore, these techniques are indispensable for judging forearm arteries as possible bypass landing sites (27).

The role of abnormal venous pressures in HAIDI is questioned. Venous hypertension by itself leads to a reduced arteriovenous 'pressure fall' and influences distal ischemia. On the other hand, a venous stenosis decreases access flow and reduces the pressure loss in the arterial tree. An angioplasty of a venous stenosis may therefore intensify HAIDI (28).

Triggers for the onset of chronic HAIDI are largely unknown. However, ischemic symptoms may initially become manifest during a dialysis session. Moreover, there is anecdotal evidence that manipulating blood flow of the artificial kidney subjectively attenuates the intensity of HAIDI associated symptoms. In **chapter 3**, ischemic symptoms, digital perfusion and skin temperature were investigated during two different regimens of blood flow (200 and 300 ml/min). The initiation of a dialysis session immediately induced a significant decrease in systemic blood pressure and finger pressure of both hands. All other variables (ischemic questionnaire scores, saturation, finger temperatures) remained stable during both regimens. Hemodialysis apparently decreases finger pressures independent of blood flow.

A decrease in blood pressure during hemodialysis is related to several factors. It is known that arterial and venous reactivity is reduced by release of nitric oxide and cytokines, dialysis membrane bioincompatibility, characteristics of the dialysate (acetate) and insufficiently increased levels of vasoconstrictors such as vasopressin (29,30). Also the temperature of the dialysate can lower blood pressure if it increases core temperature

(31). As a result, measures aimed at preventing the fall in systemic blood pressure (manipulating dialysate temperature) may also attenuate ischemic hand symptoms during a dialysis session (21,29).

SURGICAL MANAGEMENT OF CHRONIC HAIDI

Ligation of the AVF downstream of the arteriovenous anastomosis is simple and the most effective of all surgical approaches for chronic HAIDI but obviously sacrifices the access (32-40). Rarely, when a direct radial-cephalic wrist access is partially fed by an atherosclerotic ulnar artery, ligation of the radial artery distal to the arteriovenous anastomosis may abolish HAIDI (41-43) although amputation can not always be avoided (39,44). Access flow may fall considerably following such a ligation, hence its effect on perfusion pressure and flow must be studied prior to operation.

Some techniques rely on altering the position of the arteriovenous anastomosis. An anastomosis may be moved away from a larger vessel towards one of its sidebranches, i.e. the circumflex humeral artery in case of an axillary access (45). Although peripheral perfusion pressures were raised substantially, the ensuing flows (430 ml/min) were barely above thrombotic threshold levels (> 400 ml/min for PTFE graft, > 320 ml for autogenous access) jeopardizing access patency and effective dialysis (46). Interposition of a loop graft was used to correct HAIDI thus converting a direct side-to-side brachial-cephalic access at elbow level into a prosthetic brachial-basilic access. This technique creates an autogenous and a graft system that can both be used for cannulation (47,48). One study reported on ligation of a direct access at the origin of its efferent vein followed by construction of a bypass from a more distal artery towards the venous outflow tract (RUDI, revision by use of distal inflow (49).

Some techniques aimed at creating a new access situated more proximally, for example a prosthetic axillar-axillar access. Alternatively, disconnecting the arterialized vein of a brachial-cephalic access from an elbow artery and subsequent arterialization using a 4-5 mm prosthetic bypass anastomosed at a more proximal portion of the inflow vasculature (e.g. axillar artery) saves the access while HAIDI is effectively abolished (PAI, proximalization of arterial inflow) (50,51).

A popular technique for the treatment of HAIDI is DRIL (distal revascularization-interval ligation). The method assumes that HAIDI is caused by insufficient capacity of arterial collaterals to secure adequate distal limb perfusion. A standard DRIL procedure consists of two steps. The first stage entails construction of a short bypass between the artery proximal to the AVF and the brachial (or radial or ulnar) artery distal to the AVF. An autologous greater saphenous vein (GSV) bypass is preferentially used. The proximal anastomosis is located at least 3-5 cm cephalad from the anastomotic area thus avoiding the influence of the access' 'pressure sink' (12). Others have advocated the use of a 20 cm long bypass (52). The optimal distal landing site is questioned but a portion of the brachial artery is probably ideal although patent radial and ulnar arteries also serve well (10). The second stage is ligation of the feeding (usual brachial) artery just distal of the AVF thus preventing 'attraction' of blood from peripheral portions of the limb (53). The technique is also useful in leg HAIDI (15,54).

Some issues regarding the DRIL technique are incompletely understood. For instance, some patients do not require both steps. Ligating without bypassing normalized distal perfusion in a HAIDI patient (55). On the other hand, patients with distal atherosclerosis of arms (12) or legs (54) successfully received a bypass but did not require ligation. Accesses usually remain patent and usable but incidental occlusions following DRIL have been documented (56,57). Bypass patency is favourable, and DRIL appears a highly effective technique for HAIDI on both the short and medium term. Interestingly, absence of intraoperative monitoring does not influence success rates. Disadvantages include its complexity and a 10% risk for disturbed wound healing (10,27,52).

A frequently used technique for treatment of HAIDI is termed banding. Banding was introduced in the seventies (58,59), discussed in the eighties (60) and critiqued in the nineties following dismal postoperative access patency rates (15,19,33). Narrowing the access' efferent vein adjacent to the anastomosis will reduce the access flow and pressure loss associated with the AVF presence. Subsequent dilatation of the vein is prevented by applying a restrictive band of non-resorbable material: 'banding' (9,61-65). The length of the narrowed venous segment ranges from 5-30 mm. Subsequent turbulence may theoretically promote intimal hyperplasia and narrowing (28,60,66). On the contrary, effective banding of arteriovenous accesses was found to be associated with diminished intimal hyperplasia in a controlled animal model (67).

The efficacy of banding is questioned mainly because parameters guiding the grade of banding are lacking. Technical advantages of banding include its simplicity whereas the procedure can be performed under local anaesthesia. Moreover, banding is also effective in treating cardiac overload due to large access flow (51,58,68).

The aim of **chapter 4** was to investigate the existing literature on the efficacy of 'banding' for HAIDI. Interpretation of the available data indicates that a disappointing 40-60% clinical success rate was found if banding was performed without an intraoperative monitoring tool ('blind' binding), or just guided by finger pressures (19,33,39,69). In contrast, if banding was guided by flow (access or arm) or doppler measurements, total relief from digital ischemia was observed in 89% of the banded patients. Some 97% of successfully banded AVF's still functioned after a 17±3 months follow-up. The place of banding in the invasive armamentarium for HAIDI is unclear but surgical management is primarily dictated by access flow. If AVF flow exceeds 1 L/min, one may opt for banding provided that access flow and digital pressures are closely monitored intraoperatively. In contrast, if access flows are below 1 L/min, HAIDI is preferentially treated using alternative techniques including distal revascularization (DRIL) or

proximalisation of arterial inflow (PAI).
Critics worry that banding either results in access occlusion (band too tight) or in clinical ineffectiveness (band not tight enough)(70). Some (small) studies demonstrate better outcomes if banding is guided by some sort of monitoring tool. However, it is not clear which tool is the optimal guiding parameter reflecting access flow. In **chapter 5** the relation between access flow, subclavian venous saturation and finger pressures were studied during banding. Stepwise banding (25, 50, 75, and 100% reduction in access flow) in patients with HAIDI or cardiac overload (CO) demonstrated a linear decline in venous saturation and increased finger pressures (58±12 mm Hg, open AVF to 81±13 mm Hg, closed AVF). Monitoring of access flow, finger pressures and venous saturation may have the potential of guiding banding in patients with HAIDI or CO.

DOES INTRAOPERATIVE 'MONITORING' CONTRIBUTES TO SUCCESSFUL SURGERY FOR HAIDI?

Certain hemodynamic measurements that are useful in a diagnostic setting may also be helpful during corrective surgery and may aid in guiding treatment for HAIDI. Surgery is considered successful when access flow is maintained above 600-800 ml/min (AVF) or 800-1000 ml/min (graft fistula) while mean arterial finger pressures are maintained > 50 mm Hg (33). Return of palpable pulses at the wrist during a corrective procedure points towards a normalized distal perfusion (71). Increased finger pressures predicted sufficient digital perfusion (10) as did an increase of amplitude >5 mm using PVR techniques (23). Serial flow measurements of the access using Duplex ultrasound scanning contributed to effective corrective surgery in HAIDI in one patient (72). In addition, difference in flow determined in arteries of the access' upper arm and the contralateral arm allowed for effective correction in 3 other HAIDI patients (9).
The following intraoperative post-procedural clinical observations and measurements likely contribute to the success of corrective surgery in HAIDI: Pink or red coloured and warm skin of the hand, sustained capillary refill, clear palpable pulsations at the wrist, attenuated thrill over efferent vein of access, bi- or triphasic Doppler signals over wrist arteries, improved plethysmographic wave forms (PPG, PVR), augmented systolic finger pressure (> 60-70 mm Hg), digital-brachial index >0.6 (21). As most of these tools focus on improved distal perfusion, maintenance of sufficient access flow is possibly endangered. A reliable intraoperative measurement of access flow is a requisite for guiding surgical decisions during surgery for HAIDI.
Chapter 6 reports the short and long term clinical efficacy of banding procedures using intraoperative measurements of access flow, finger pressures and subclavian venous saturation in HAIDI and cardiac overload (CO) patients. Banding reduced access flow by two liters per minute (3.2±0.3 l/min to 1.2± 0.1 l/min) in CO patients. The DBI (digital brachial index) in HAIDI patients increased significantly from 0.52±0.08 to 0.65±0.08

(<0.6 is considered critical). Ischemic scores using the questionnaire in these patients diminished from 153±33 to 42±15, the latter values are not different when compared to a general dialysis population (range 35-50) (73). All patients successfully continued dialysis, and no banding related complications were found. After a mean follow up of 30 months, mean access flow was 1.0 L/min in surviving patients. Banding for HAIDI and CO guided by intraoperative measurements of access flow, finger pressures and subclavian venous saturation is effective on the short and long term.
Access flow is related to systemic blood pressure. General or locoregional anesthesia may result in a drop in blood pressure due to (local) vasodilatation. It is important to take these altered values into account during a banding procedure guided by flow measurements. It is probably more accurate to maintain the blood pressure at the patient's normal level during corrective surgery. Otherwise, banding may lead to too high postoperative access flows. Further investigations have to be performed whether banding is more accurate if blood pressure is maintained at a normal level.

SURGICAL MANAGEMENT: AMPUTATION

Patients require acute limb amputation in the presence of HAIDI if uncontrollable gangrene and associated sepsis is at hand. Some studies found amputations in early occurring HAIDI only (74) whereas others exclusively reported amputations in HAIDI developing several years after initiation of hemodialysis (57,75). A history of longstanding diabetes and previous amputation of other parts of limbs are strong risk factors for a HAIDI-related amputation (75). Amputation without an attempt to improve distal perfusion in case of ongoing digital or limb gangrene rarely succeeds in a cure (76).

IS TIME OF ONSET OF HAIDI RELATED TO TYPE OF AVF ?

Studying the literature on the incidences of hand ischemia in the presence of a hemodialysis access is hampered by heterogenicity. However, factors that predispose for HAIDI are diabetes mellitus (56,77), female gender (1,22,77), hypertension (19,56), coronary artery disease (78), multiple access surgical procedures, peripheral arterial obstructive disease (56), and smoking (15). Although any type of AVF can cause HAIDI, several locoregional risk factors promote HAIDI such as using brachial arteries as inflow source of the access (77,79), use of an AVF in the lower limb (54), and a large diameter arteriovenous anastomosis (80). Configuration of the arteriovenous anastomosis may also determine the occurrence of ischemia as a side-to-side radiocephalic access demonstrates HAIDI more often when compared to the end-to-side type (41,81). Altering the anastomotic angle between vein and artery is also thought to influence the onset of HAIDI (82).

Tapered grafts were hypothesized to harbour a smaller risk on distal ischemia but disappointed (10,15,19). Most authors advice a maximal anastomotic diameter of 6-8 mm near the wrist joint, and of 5-7 mm at elbow level, respectively (69,80,83). The use of proximal segments of radial or ulnar arteries instead of the cubital brachial artery for elbow AVFs prevented HAIDI effectively (84,85).
An overall classification of chronic HAIDI is currently lacking. Patients may be distinguished according to time of onset as acute (86), subacute (87) or chronic (88). However, it is not clear if time of onset of ischemia is related to type of AVF. **Chapter 7** reviews the literature on this relationship. If hemodialysis-induced hand ischemia is acute (<24 hours after AVF creation), almost 90% harboured a nonautogenous AVF. In contrast, chronic HAIDI (>1 month after AVF insertion) is generally related to a maturing autogenous elbow AVF. The evolution of chronic HAIDI closely resembles sequelae that are observed during progressive PAOD (peripheral arterial occlusive disease). A novel classification for HAIDI is proposed that is based on the grade 1-4 universally accepted Fontaine system for PAOD. Standardisation according to this novel classification allows for comparison of incidences and management for chronic HAIDI.

IS THERE ROOM FOR ENDOVASCULAR MANAGEMENT OF CHRONIC HAIDI?

Studies performed in average dialysis populations report an incidence of HAIDI requiring surgery ranging from 0 (89-91) to 9% (33,92-95). Some studies reported even higher incidences up to 17% (22) and even 33% (54), depending on population characteristics, operative tactics and index of suspicion for HAIDI. Generally, about 4-7% of all patients belonging to a mixed dialysis patient population requires surgical intervention for HAIDI. Surgery is mandatory in chronic HAIDI with rest pain or gangrene in relatively healthy individuals.
Prior to embarking upon invasive evaluations, it must be established whether salvage of the causative access is mandatory. Alternative dialysis treatments including catheter access or peritoneal dialysis are worthwhile exploring. Several questions need answering. Are conditions in the contralateral arm favourable for creation of an uncomplicated access? How is the causative access functioning? If the access is working properly (also as judged by the nursing staff), and other options for treatment are unfavourable, HAIDI should be treated with a corrective technique that does not endanger the access. One must also realize that patients with HAIDI belong to a selected population with a limited life expectancy as mortality rates up to 35% in the first 6 postoperative months following corrective vascular surgery have been reported (52,76,96).
Prior to surgery, the arterial inflow tract is checked for localized stenotic lesions. Hemodynamic significant lesions should be treated by PTA and/or stenting. The distal arterial tree up to the digital arteries is thoroughly examined angiographically, ideally while providing manual compression of the venous outflow. Surgical treatment is subsequently indicated in the absence of inflow lesions or when successful endovascular treatment does not abolish invalidating or limb threatening HAIDI.

RARE CONSEQUENCES OF CHRONIC HAIDI

Over the years, we have observed two patients with HAIDI that are described as separate cases. **Chapter 8** reports on a 14-year old girl with HAIDI who demonstrated retarded growth of the AVF hand 5 years after a successful kidney transplantation. Her AVF was not ligated. Access flow was 1400 ml/min and finger pressures were low. A stenotic brachial artery was found using angiography but angioplasty did not resolve the stenotic lesion. A reversed blood flow ('steal') in the radial artery was demonstrated by duplex ultrasound. Her ischemic symptoms eventually disappeared after AVF ligation. It is thought that an impaired arterial inflow combined with a low resistance elbow AVF may have resulted in a chronically diminished nutritive hand perfusion and consequent growth retardation. In children with a well functioning renal transplant and a patent elbow AVF, access ligation is advised if distal tissue perfusion is diminished.
Long term immunosuppression following organ transplantation is known to promote the onset of skin cancers (97). However, the effects of chronic regional ischemia on skin abnormalities are unknown. In **chapter 9** a renal transplant patient on prolonged immunosuppression is described who developed multiple well differentiated squamous cell carcinomas (SCC) in an ischemic and atrophic HAIDI hand. Finger pressures were unmeasurably low. Seldinger angiography excluded stenotic lesions or occlusions in the arterial tree but the hand itself was poorly perfused. During intraoperative clamping of the AVF the finger pressures remained unaltered. Additional banding was therefore aborted. It is hypothesized that local oxidative stress (HAIDI) may act as a co-carcinogenic factor for the development of SCC in renal transplant patients receiving immunosuppressive agents.

BANDING AND CARDIAC OVERLOAD

The incidence of HAIDI will rise in the coming decade as a result of the popularization of elbow AVF's as promoted by KDOQI and other guidelines. Our HAIDI patients with refractory disease received surgery after a mean of 17 months following AVF construction. An unknown number of autogenous AVF's will demonstrate ongoing maturation over the years to come, and their owners may subsequently develop a high flow access (HFA) and associated cardiac overload (CO). Patients in the present thesis were operated for CO some 8 years after routine AVF-construction (20). In **chapter 10** a review of the literature is provided on pathophysiology, diagnosis and treatment of a HFA. The pathophysiology of CO is multifactorial but these events may lead to left ventricular hypertrophy (LVH), progressive cardiac failure and death. There is evidence showing reversibility of LVH after sacrificing an HFA. Various alternative flow measurement techniques may diagnose HFA, and cardiac investigations may be required to identify ventricular hypertrophy. Clearly defined criteria for the treatment of HFA are currently lacking. The banding technique is a simple and effective method for the treatment of HFA-associated CO provided that access flow is intraoperatively monitored.

CONCLUSIONS OF THIS THESIS

1. Mild to moderate (grade 1-2) HAIDI is frequently present in patients with an autogenous elbow fistula.
2. The efficacy of banding is optimized if the operation is guided by intraoperative measurement of access flow and finger pressures. The technique is effective in 89% of the patients whereas the AVF remains patent in 97% after 17 months of follow-up.
3. Access flow, central venous saturation and finger pressures are interrelated. Alterations in these parameters are useful in guiding banding in patients with HAIDI and CO.
4. Flow and finger pressure guided banding is an effective treatment of HAIDI and CO, both on the short and the long term.
5. Intradialysis exacerbation of HAIDI is related to systemic hypotension. Manipulating artificial kidney blood flow does not alter the finger's temperature or finger pressure at the AVF side.

SOME THOUGHTS ON THE FUTURE

The general aim of studies that are presented in this thesis is to expand the knowledge on hemodialysis access induced distal ischemia (HAIDI). Symptoms and signs of HAIDI apparently are universally present in an average dialysis population. Severe chronic HAIDI (grade 3-4) is easily diagnosed. However, a mild to moderate grade 1 or 2 ischemia is not, possibly because patients are reluctant to report symptoms. Some patients may experience intensification of hand pain only during a hemodialysis session but may think that these feelings of pain and coolness are 'part of the game'. A moderate type of HAIDI may progress towards a third or even fourth grade. Care providers have the responsibility to identify HAIDI in an early stage as proper treatment may prevent serious sequelae of chronic ischemia. How can an early diagnosis be facilitated? Patients with risk factors for HAIDI (diabetes, females, multiple surgical procedures, autogenous elbow AVF) may be asked to score the ischemic questionnaire on a regular basis, for instance once every two months. Gradual higher scores may prompt the staff to perform a thorough physical examination of the hand and to measure finger pressures. The threshold for a subsequent magnetic resonance or Seldinger angiography must be very low or non-existent.

The body of literature on diagnosis and treatment of HAIDI is limited (<200 hits on PubMed). Randomized trials are absent. For instance, some investigators are 'believers' of banding, whereas others prefer a DRIL or a PAI. The absence of powered trials is probably due to the (alledged) restricted number of patients. However, it should be anticipated that their numbers will increase dramatically in the coming decade. First, DOQI stimulates construction of autogenous elbow AVFs. This type of access is inherently associated with a reduced risk of occlusion whereas it requires marginal maintenance compared to a graft. The downside of an optimal longevity of an elbow AVF is the progressive risk of HAIDI (mostly after one or two years). Moreover, as the life expectancy of hemodialysis patients will continue to increase, a progressively larger group of patients will also live long enough to develop cardiac overload due to inappropriate AVF maturation. In the near future, care providers must be prepared to treat increasing numbers of patients with HAIDI and CO. One may consider starting therapy in an earlier stage or even 'pre-emptive'.

Proper management of HAIDI starts with a conservative or endovascular measure. Only if these treatments fail, a HAIDI patient should undergo vascular surgery. Banding in the present studies was performed in a fully anaesthetized patient. This approach was used as it is thought that successful banding requires a stable signal of access flow and therefore total absence of arm movements. We are convinced that the success of banding procedures heavily depends on the pivotal role of correct flow monitoring. However, systemic blood pressure (and associated regional blood flow) during general anesthesia is considerably lower compared to values observed in a conscious state. Although the current flow probes may be sensitive to movement artifacts and were therefore stabilized on the operation table, a next generation of flow probes (OptiMax Flowprobes, Transonic, figure 1 and 2) allows a stable fixation on the arm itself. By using these novel probes, an optimally stable access flow signal is guaranteed in an awake patient. Banding procedures for HAIDI or CO will therefore be possible using a local or locoregional technique in an outpatient setting. In fact, the last three patients that received a banding procedure in the Máxima Medical Center were operated using a local anesthetic technique only. No additional regional or systemic anesthetic agents were required for a successful procedure in either patient.

Figure 1 *Optimax flow probes allow accurate banding using local anesthetics only.*

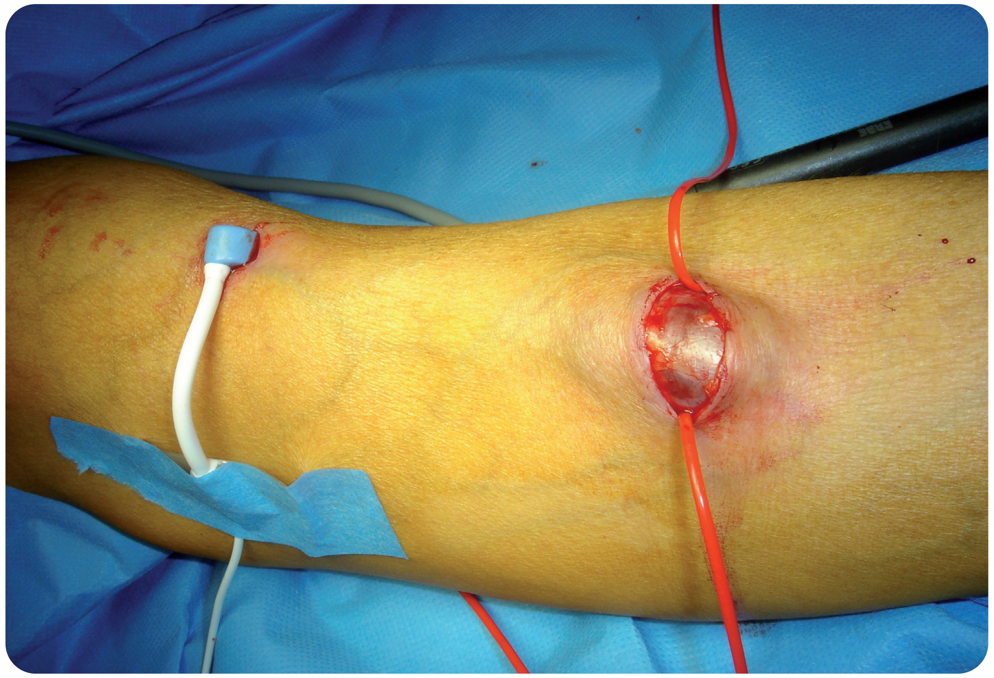

Figure 2 *Optimax flow probes allow accurate banding using local anesthetics only.*

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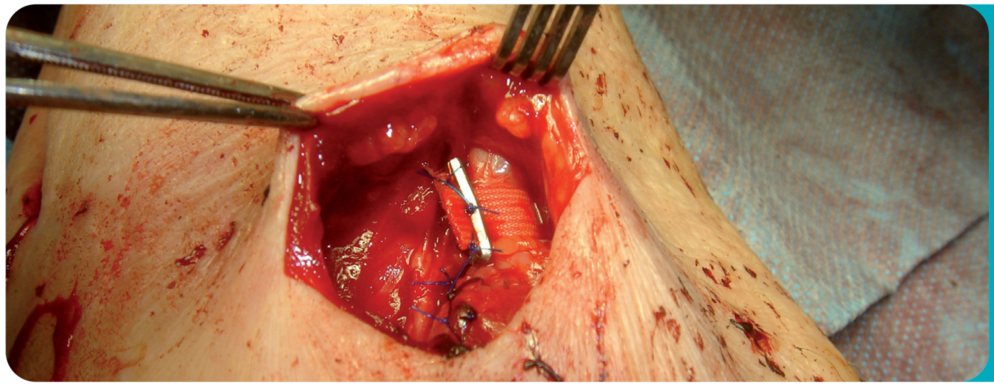
CHAPTER 12



Nederlandse samenvatting (Summary in Dutch)

INLEIDING

Sommige patiënten met nierfalen zijn afhankelijk van hemodialyse (bloedspoeling) via een zogenaamde 'shunt' (AVF, arterioveneuze fistel) in de arm. Bij een deel van hen ontstaat een doorbloedingsvermindering van hun 'shunthand' (HAIDI, hemodialysis access induced distal ischemia). Het hoofddoel van dit proefschrift was om diverse aspecten van HAIDI nader te bestuderen.
In de bestaande literatuur wordt een aantal afkortingen gebruikt voor het fenomeen 'handischemie bij hemodialyse'. Vaak wordt de term 'steal' gebezigd, hetgeen niet correct is. Immers, per definitie veronderstelt steal een omgekeerde richting van de bloedstroom in de aanvoerende arterie (dus van de hand af in plaats van naar de hand toe). Een bekend voorbeeld van 'steal' wordt gezien bij het 'subclavian steal syndroom', waarbij de stroomrichting in de arteria vertebralis van de hersenen af is, met verminderde breinperfusie als gevolg. Echter, bij HAIDI wordt nagenoeg altijd een voorwaartse flow waargenomen, en is het steal-fenomeen zelden aanwezig. Omgekeerd wordt steal nog wel eens gezien bij individuen met een hemodialyseshunt die helemaal geen symptomen van handischemie vertonen. Zowel steal als HAIDI wordt zelden tegelijkertijd bij een individu vastgesteld.
Maar welk pathophysiologisch ontstaansmechanisme ligt wel ten grondslag aan HAIDI? Chronische HAIDI bij langdurige hemodialyse ontstaat door een geleidelijke afname in arteriële vaatelasticiteit gekoppeld aan een AVF met allengs lager wordende weerstand in het afvoerende veneuze stelsel. Deze combinatie leidt tot een geleidelijke afname van de perfusiedruk naar de hand. Anders geformuleerd, naar perifeer toe blijft er steeds minder bloeddruk over om de dialysehand adequaat van bloed te kunnen voorzien.

In **hoofdstuk 1** wordt op algemene aspecten van HAIDI ingegaan. De literatuur wordt onderzocht op veel voorkomende anamnestische gegevens, risicofactoren, symptomatologie, lichamelijke tekenen, aanvullend onderzoek en behandelingsvormen. Bij HAIDI wordt door patiënten met name gerapporteerd over koude van hand/vingers, pijn, krampen, verminderd gevoel en krachtsverlies in de AVF-hand/onderarm. In **hoofdstuk 2** wordt een vragenlijst geïntroduceerd waarin deze symptomen worden gemeten en gekwantificeerd. Twee populaties van hemodialysepatiënten (n=120) scoorden met behulp van een visual analog scale (mininaal 0 punten, maximaal 10) ernst en frequentie van iedere met HAIDI geassocieerde klacht. De groep bestond uit patiënten met 3 soorten AVF's (RC, radiocephalic, ofwel polsshunt; BC, brachiocephalic, elleboogsshunt; 'Loop', kunstader). De voornaamste bevinding was, dat met name de BC-groep veel tekenen van HAIDI vertoonde (79% minimaal een van de 5 genoemde klachten). Aan deze ischemie-enquete zal in dit proefschrift met regelmaat worden gerefereerd. Ook werd deze vragenlijst gebruikt om een 'HAIDI-symptomatische' subgroep te identificeren. Bij lichamelijk onderzoek van 14 voor HAIDI verdachte hemodialysepatienten waren er aan de AVF-arm vaak verminderde pulsaties voelbaar over de arteria radialis. Tevens was de huid van handpalm en -rug veelal kouder ten opzichte van de andere zijde. Bij temperatuurmetingen bleek de huid op de top van de wijsvinger inderdaad 1 graad Celcius lager te zijn. Ook was de kracht van de AVF arm 20% minder dan de andere kant. Vingerbloeddruk bleek ook aanzienlijk lager (40%) aan de AVF zijde. Wanneer de AVF werd afgedrukt, normaliseerden deze vingerdrukwaarden. Een positieve 'compressie-test' bij een patient met HAIDI heeft een duidelijke klinische betekenis. Het betekent dat lagere vingerdrukken in dit geval niet gefixeerd maar reversibel zijn, en dus behandelbaar.

Sommige patiënten gaven aan, thuis weinig klachten van HAIDI te hebben. Echter, ze voelen meer pijn en koude tijdens een dialysesessie, met name als de bloeddoorstromingssnelheid naar de dialysemachine hoog is. In **hoofdstuk 3** wordt de hypothese getest, dat de intensiteit van HAIDI-klachten gerelateerd is aan deze 'dialysemachine-snelheid'. Tijdens dialysesessies met twee snelheden (flow 200 ml/min of 300) werden bloeddruk, hartslag, vingerdrukken, -temperatuur, saturatie en HAIDI-scores gemonitored. Opvallend was dat er direct na het starten van de dialyse een significante bloeddrukdaling en ermee geassocieerde vingerdrukdaling optrad. Andere parameters bleven stabiel tijdens beide 3-uur durende dialysesessies. Bij verergering van de HAIDI klachten rondom een dialyseperiode dient behandeling gericht te zijn op het voorkomen van een dalende bloeddruk.

Voor de conservatieve behandeling van HAIDI worden verschillende methoden beschreven, echter deze blijken zelden afdoende. Vaak moet er dus (endo) vasculair worden ingegrepen. Diverse technieken worden gepropageerd waaronder 'banding', handrevascularisatie (DRIL, distal revascularization-interval ligation), of het aanleggen van een meer okselwaarts gelegen anastomose (PAI, proximalization of arterial inflow). Bij banding wordt met hulp van een kunststof bandje de afvoerende vene van de AVF vernauwd. Zodoende ontmoet het bloed in de AVF meer 'weerstand' waardoor een grotere arteriële flow bij voorkeur naar de hand ontstaat. Echter, velen beschouwen banding als een controversiële techniek aangezien er vaak AVF-occlusies zijn beschreven (bandje te hard aangetrokken). Niet zelden bleek banding onvoldoende effectief (bandje niet hard genoeg aangetrokken). In **hoofdstuk 4** wordt in een overzichtsstudie de resultaten van in de literatuur gepubliceerde bandingprocedures bij patiënten met HAIDI kritisch beschouwd. Zij die 'blind' werden geband (zonder peroperatieve monitoring van bijvoorbeeld AVF-flow of vingerdrukken) schoten over het algemeen weinig op met de operatie (< 50% succes). Echter, banding bleek wel succesvol (90%) indien tijdens de operatie metingen van AVF-flow werden gecombineerd met bijvoorbeeld 'terugkerende pulsaties van de arteria radialis', of met 'toegenomen vingerdrukken'. De lange termijn

patency van de groep succesvol gebande AVF was zeer gunstig (97%, follow-up 17±3 maanden).

De bestaande literatuur betreffende HAIDI toont aan dat er weinig meetmethodes zijn die de mate van handischemie bij hemodialyse nauwkeurig weergeven. Het doel van **hoofdstuk 5** was om diverse parameters tijdens bandingprocedures te meten. Wij veronderstelden dat het stapsgewijs verminderen van de AVF-flow tijdens banding een duidelijk effect zou hebben op de centraal veneuze saturatie alsmede (plethysmografisch gemeten) vingerdrukken. Deze hypothese werd getoetst in hemodialysepatienten met HAIDI of met cardiac overload. Een deel van hemodialysepatienten ontwikkelt namelijk op termijn soms ook een hoge flow in de shunt hetgeen kan leiden tot chronische cardiale overbelasting (cardiac overload, CO). Tijdens het banden daalde de zuurstofsaturatie in de CO-groep van 93±2% (100% open AVF) naar 80±3% (100% dicht). De HAIDI groep liet eveneens een, weliswaar kleinere, significante daling zien (88±1% naar 84±2%). Vingerdrukken (en afgeleide digital brachial index (DBI) stegen lineair in beide groepen bij stapsgewijs comprimeren van de AVF. Bij HAIDI was dit 58±12 mmHg naar 81±13 mmHg, terwijl de DBI steeg van 0.54±0.08 naar 0.72±0.10. In de CO groep lagen deze waarden hoger (79±13 mmHg vs 102±9 mmHg). Er bestond een lineaire correlatie tussen AVF flow en centraal veneuze saturatie, met name bij de CO-groep (r^2 = 0.96). Deze studie toont aan dat er een dosis-afhankelijke relatie bestaat tussen AVF flow, centraal veneuze saturatie en vingerdrukken. Veranderingen in deze parameters kunnen in potentie de chirurg van dienst zijn bij het peroperatief bepalen van de mate van banding bij operaties voor HAIDI of CO.

In **hoofdstuk 6** worden de korte- en lange termijns resultaten van banding op basis van flow-, saturatie- en vingerdrukmonitoring bij patienten met CO (n=8) of HAIDI (n=9) beschreven. Banding verlaagde de AVF flow bij CO van 3.2±0.3 l/min naar 1.2±0.1 l/min. Bij patiënten met HAIDI verbeterde de DBI van 0.52±0.08 tot 0.65±0.08. De door de vragenlijst verkregen 'ischemie-score' in deze laatste patiëntengroep daalde van 153±33 naar 42±15 hetgeen aangeeft dat ze veel minder last van HAIDI overhielden. Alle patiënten konden na de operatie direct weer hemodialyseren. Een patient moest 2.5 jaar na de eerste ingreep weer geopereerd worden in verband met een wederom te hoge flow (>2 l), waarvoor opnieuw een banding werd verricht met goed resultaat. Een andere CO patiënt had onvoldoende flowdaling, waarvoor opnieuw eenzelfde procedure werd verricht met uiteindelijk wel een goed resultaat. Na een follow-up duur van gemiddeld 30 maanden was de AVF flow in nog levende patiënten (n=11) acceptabel (1.0±0.1 l/min).

Chronische HAIDI komt het meest frequent voor bij autologe elleboogs-AVF's. Echter, het is onduidelijk of er een relatie bestaat tussen tijdstip van ontstaan en ernst van HAIDI enerzijds, en soort en positie van hemodialyseshunt anderzijds (autoloog, kunst;

elleboog of pols). In **hoofdstuk 7** werd een literatuurstudie hierover verricht. HAIDI werd geclassificeerd als acuut (<1 dag na aanleggen van een AVF), subacuut (<1 maand), en chronisch (>1 maand). Er werden 21 studies gevonden die aan gestelde criteria voldeden voor een chirurgische of percutane behandeling van HAIDI (n=464 patienten). Acute HAIDI bleek in 88% van de gevallen te ontstaan na implantatie van een kunststof vaatprothese. Chronische HAIDI daarentegen werd voornamelijk (91%) gevonden bij zich ontwikkelende autologe elleboogs-AVF's. Gemiddeld duurde het 16±3 maanden voordat chronische HAIDI chirurgisch werd gecorrigeerd. Er werd een classificatie voorgesteld die ernst van chronische HAIDI eenvoudig beschrijft in analogie van de Fontaine classificatie bij perifeer arterieel vaatlijden (HAIDI graad 1-4b). Gestandaardiseerde rapportage maakt het mogelijk om studieresultaten onderling goed te kunnen vergelijken.

Terminale nierinsufficiëntie is zeldzaam bij kinderen, en HAIDI als complicatie van een AVF is nauwelijks beschreven. **Hoofdstuk 8** rapporteert over een patiënte van 14 jaar met ernstige HAIDI en een opvallend kleinere en pijnlijke dialysehand. Na succesvolle niertransplantatie op 9-jarige leeftijd was haar AVF niet opgeheven. De groeiachterstand van de dialysehand bleek het gevolg van een vernauwde arteriele aanvoer in combinatie met een omgekeerde flow in de aanvoerende arteria radialis ('true steal'). Na ontkoppelen van de AVF werd zij klachtenvrij. Het lijkt raadzaam om kinderen met een goede niertransplantaatfunctie en een open AVF te controleren op groeiontwikkelingsstoornissen of HAIDI klachten, en bij twijfel de AVF op te offeren.

Langdurig gebruik van immunosuppressie na orgaantransplantatie gaat regelmatig gepaard met het ontstaan van huidtumoren. In **hoofdstuk 9** wordt een niertransplantatiepatiënt beschreven die een extreem pijnlijke atrofische HAIDI-hand had ontwikkeld met een 5-tal plaveiselcelcarcinomen. Zijn AVF was fors gedilateerd maar werd in ere gehouden in verband met verslechterende transplantaatfunctie. Hij gebruikte al meer dan 25 jaar prednison en imuran. De andere hand was goed doorbloed en onpijnlijk zonder huidafwijkingen. Zowel een Seldinger angiografie als vingerdrukmetingen lieten ernstige perfusiestoornissen zien van de voormalige dialysehand en vingers. Er wordt verondersteld dat het carcinogene effect van immunosuppressiva door langdurige ischemie plaatselijk kan worden versterkt.
Arteriële aanvoer en veneuze afvoer van autologe AVF's kunnen op termijn zodanig dilateren dat er permanent hoge flows in de shunt ontstaan. Deze verhoogde flows vormen een alsmaar grotere belasting voor het cardiopulmonale systeem. Indien AVF flows langdurig >2 l/min bedragen, lijkt het raadzaam om chirurgisch in te grijpen. **Hoofdstuk 10** beschrijft diverse aspecten van de 'high flow access' en de chirurgische behandeling door middel van banding. Hoewel het aantal voor deze indicatie gebande patiënten in de beschreven literatuur klein is (n=44), blijkt op middellange termijn (follow-up gemiddeld 11 maanden) de effectiviteit gunstig. Een voorwaarde is, dat de

mate van banding wordt gemonitored en bepaald door peroperatieve flowmetingen. Immers, indien de trombosedrempel wordt overschreden (flow < 300 ml/min), zal de kans op AVF occlusie toenemen.

Dankwoord

DANKWOORD

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Curriculum Vitae

CURRICULUM VITAE

Frank van Hoek was born in Hengelo (Overijssel) in the Netherlands on May 30th 1972. He attended secondary school in Hengelo (MAVO Driener-es, HAVO and Atheneum, Bataafse Kamp) where he graduated in 1992.
In that same year he started his medical studies at the University of Nijmegen. During this period he became a member of the medical society SO.DA.NO.GO. After graduating from medical school in 1996, he participated in a research project on “Clinical and motility aspects of functional constipation” (dr. R.M.H.G. Mollen). This brief encounter with science fuelled his research interests. In September 1999 he completed his medical studies and held consecutive positions as a non-training registrar at the emergency department of the Canisius-Wilhelmina Hospital in Nijmegen, the departments of General Surgery at St Joseph Hospital in Veldhoven and Radboud University Nijmegen Medical Centre, respectively. In January 2002 he started his surgical residency in Máxima Medical Center (formerly St Joseph Hospital) in Veldhoven (dr. F.A.A.M Croiset van Uchelen and dr. R.M.H. Roumen). The final year of his 6 year residency was completed at the department of Vascular Surgery at the Radboud University Nijmegen Medical Centre (Prof. dr. R.P. Bleichrodt, dr. J.A. van der Vliet).
All studies presented in the present thesis were performed in the Máxima Medical Center and were started at the beginning of his surgical residency.
After graduating as a general surgeon in January 2008 he continued his training as a CHIVO (CHirurg In Vervolg Opleiding, Surgeon’s subspecialisation) in Vascular Surgery at the Catharina Hospital in Eindhoven (dr. J. Buth, dr. M.R.H.M. van Sambeek). As of July 2009 he works as a vascular surgeon in the staff of the Radboud University Nijmegen Medical Centre.
He is married to Monique Prickarts and they have three children: Mirthe (2002), Tim (2004) and Rik (2006).