Acknowledgement

TransonicSystems’ gratefully acknowledges Dr. Frank van Hoek for his permission and willingness to allow Transonic Systems Inc. to publish this synopsis of his PhD thesis.

Chapter I includes, in its entirety, Dr. Frank van Hoek’s introduction to HAIDI. Chapters 2-10 comprise Transonic synopses of his peer-reviewed published studies that make up the body of the thesis. These studies took place at Maxima Medical Center, Veldhoven, The Netherlands.

Chapter 11 presents Dr. van Hoek’s discussion, conclusions and future perspectives on HAIDI, along with a comprehensive list of references. Dr. van Hoek’s curriculum vitae concludes the booklet.

It is our hope that those who treat HAIDI patients will find Dr. van Hoek’s work insightful and educational in advancing understanding of this difficult condition that afflicts a number of hemodialysis patients.

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# Hemodialysis Access-Induced Distal Ischemia (HAIDI)

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Introduction, Aims and Outline

If a patient progressively suffers from end-stage renal disease, hemodialysis is lifesaving. 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 neighboring 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 200ml/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 loco regional (cerebral) ischemia. Only when a compensatory increase of cerebro petal 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 brachiobasilic 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.
Introduction, Aims and Outline cont.

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 maybe due to the absence of intra-operative monitoring techniques guiding a banding procedure. A systematic literature search on efficacy of banding in relation to intraoperative 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.
Introduction, Aims and Outline cont.

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.

Chapters 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.

References
Introduction, Aims and Outline cont.


Chapter 2: Steal in Hemodialysis Patients Depends on Type of Vascular Access

(Transonic Systems Synopsis)

Objective
- To study the incidence and severity of steal phenomena in hemodialysis patients with brachiocephalic AV fistula, radiocephalic fistula, and prosthetic forearm loop fistula vascular access.
- To investigate possible diagnostic tools for detecting steal.

Study
A subgroup of patients was identified as having steal through a questionnaire generated through literature related to steal in the presence of a dialysis fistula. Physical examination, arterial blood pressure, skin temperature, digital oxygenation, grip strength and plethysmography were used to detect steal. Contralateral arm measurements provided control values.

Results
- 120 patients completed the questionnaire.
- Type of access did not influence frequency and severity of reported steal.
- Cold hands were 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 noted as being at risk for steal (p<0.01).
- Intensity of steal was not related to magnitude of access flow.
- Digital skin temperatures and grip strength were lower in hands with steal (P<0.02). Manual compression of the AVF normalized 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 were common in hemodialysis patients. Patients with a BC were 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.
**Chapter 3: Hemodialysis Decreases Finger Pressures Independent of Artificial Kidney Blood Flow**

(Transonic Systems Synopsis)

**Objective**
To study the effects of altered blood flow on ischemic symptoms, digital perfusion and finger temperature in hemodialysis patients and to compare the effects of two different regimens of arterial blood flow in patients with an arteriovenous fistula (AVF).

**Study**
- Ten patients were identified by the questionnaire as those who subjectively experienced ischemic symptoms during hemodialysis.
- Ischemic symptom score, systolic blood pressure, heart rate, oxygen saturation, finger pressure (Pdig), and finger temperature (Tdig) were used for the measurement protocol and were monitored during two different arterial blood flow dialysis sessions (prior to dialysis, after 60, 120, 180 min, and immediately after discontinuation).

**Results**
- Prior to dialysis, Finger Pressure (Pdig) and Finger temperature (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.
Objective
To investigate the short and long term efficacy of banding for refractory HAIDI

Study
• Medical literature published between 1966 and June 2008 was identified for the study and the role of surgical banding for refractory hemodialysis access-induced distal ischemia (HAIDI) was systemically reviewed (39 articles).
• “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.

Results
If banding is executed without the guidance of 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).

Conclusion
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.
Chapter 5: Access Flow, Venous Saturation and Distal Pressures in Hemodialysis


Objective
To identify objective parameters that reflect AVF flow in hemodialysis patients with access related Cardiac Overload (CO) or Dialysis-Associated Steal Syndrome (DASS) requiring corrective surgery.

Study
Patients underwent serial measurements of subclavian venous saturation ($\text{Sat}_{\text{ven}}$), access flow ($\text{Flow}_{\text{us}}$) and index digital pressures ($\text{P}_{\text{dig}}$) during a corrective banding procedure. A total of 273 AV-access cases performed between January 2003 and April 2006 were analyzed for this study. Patients received access surveillance with regular measurements of blood flow and venous pressures. $\text{Sat}_{\text{ven}}$, $\text{Flow}_{\text{us}}$ and $\text{P}_{\text{dig}}$ were measured.

Results
- Data were gained from 14 patients (9 males, mean age=53±6 years) during 6 studies (CO n=8, DASS n=8).
- Mean pre-operative systolic blood pressure in awake patients was 148±8 mmHg (CO group) and 156±20 (DASS group).
- Intra-operative blood pressure during general anesthesia was 106±9 (CO group) and 97±6 mmHg (DASS group).
- Correlations between $\text{Flow}_{\text{preop}}$ or $\text{Flow}_{\text{us}}$, $\text{Sat}_{\text{ven}}$, and $\text{P}_{\text{dig}}$ prior to banding were not significant in CO or DASS group.
Chapter 6: Banding of Hemodialysis Access to Treat hand Ischemia or Cardiac Overload

van Hoek F, Scheltinga M, Luirink M, Pasmans H, Beerenhout C,
(Transonic Systems Synopsis)

Objective
To investigate short and long-term efficacy of banding in patients with Cardiac Overload (CO) or Hemodialysis Access-Induced Distal Ischemia (HAIDI).

Study
• Study participants had at least three consecutive access flows ≥ 2.0 l/min, or experienced symptomatology of invalidating hand ischemia and objective signs of hypoperfusion (mottled skin, ulcers, low digital pressure).
• 17 patients underwent banding procedures (n=19).
• Parameters including access flow, digital brachial index (DBI) and symptomatology of hand ischemia using a standard scoring system were determined before and after the banding procedure.

Results
• 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).
• Flow\textsubscript{preop} in patients with CO was nearly 1.2 liter more than compared to the patients with hand ischemia (3.2 ± 0.3 l/min vs 2.0 ± 0.3 l/min, p<0.001)
• Surgical banding in CO patients (n=9) decreased access flows by 2 ltr (Flow\textsubscript{preop} 3.2 ± 0.3 l/min vs Flow\textsubscript{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). On the other hand, ischemic symptomatology was diminished (from 153 ± 33 to 42 ± 15, P<0.02).
• No complications including wound infections, operative morbidity or mortality were noticed.
• All patients successfully continued dialysis immediately after banding and no immediate access occlusions were found (< 3 months).
• 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.
Chapter 7: Time of Onset in Hemodialysis Access-Induced Distal Ischemia (HAIDI) is Related to Access Type

Scheltinga MR, van Hoek F, Bruijnincx CM, Nephrology Dialysis and Transplantation, 2009; 24(10): 3198-204. (Transonic Systems Synopsis)

Objective
To investigate if a relationship is present between type of AVF and time of onset and intensity of HAIDI.

Study
Time of onset of HAIDI was categorized as ‘acute’ (re-operated within 24 hours after routine AVF creation), ‘subacute’ (later than 24 hours after first AVF creation) and ‘chronic’ (after one month). Type of HAIDI in relation to access type, location and follow up were tabulated.

Results
• The data from 21 studies on patients (n=464) undergoing surgical or percutaneous correction were analyzed and fulfilled the inclusion criteria.
• Acute ischemia was diagnosed in 22% (104/464) and 87% of these acute ischemia patients had undergone a nonautogenous AVF.
• Patients who underwent an operation later on in the first postoperative month for subacute HAIDI had an autogenous elbow AVF (79%, 77/97).
• Chronic HAIDI was predominantly associated with an autogenous AVF at elbow level (91%, 212/232).

Conclusions
• Early hand ischemia after routine access surgery is usually related to grafts and not to autogenous access creation.
• If patients have several risk factors for acute hand ischemia, such as diabetes, clinicians may wish to consider an autogenous AVF.
• A disadvantage of an autogenous access is its association with chronic hand ischemia, particularly if the access was created with a brachial artery.
Chapter 8: Retarded Hand Growth Due to a Hemodialysis Fistula in a Young Girl

van Hoek F, Scheltinga MR, Krasznai AG, Cornelissen EA, Pediatric Nephrology 2009 Oct;24(10): 2055-8
(Transonic Systems Synopsis)

Case Report

Patient: 14-year old female with symptomatic hand ischemia due to a patent brachio-cephalic AVF 5 years after successful kidney transplantation.

Presentation: Patient had been diagnosed with progressive kidney failure at four due to segmental glomerulosclerosis. She began hemodialysis through a left brachiocephalic elbow AVF when she was eight years old.

A four cm proximal left brachial artery stenosis was diagnosed 8 months after hemodialysis initiation. Percutaneous transluminal angioplasty (PTA) was performed twice but was not effective. At nine years of age, she had a successful kidney transplant, but her patent left AVF was not ligated.

Five years later, after complaints of left arm and hand pain, an exam revealed left arm or hand ischemic symptoms: an aneurysmatic AVF with intense thrill; significantly smaller left hand; no left radial artery pulsation; decreased left lower arm and hand strength; and a diminished palm sensibility. Access flow was 1,400 mL/min and the ischemic score was 87. A stable brachial arterial stenosis was detected. HAIDI, associated with delayed limb growth, was diagnosed and followed by access ligation and physical therapy. One year after the operation, the girl no longer presented with ischemic symptoms.

Discussion

• Distal hypotension due to an impaired arterial inflow combined with a low resistance elbow AVF may result in chronic hypoperfusion of acral portions and growth retardation of an extremity.

• Persistent high access flow may result in cardiac overload and failure due to left ventricle dilatation and hypertrophy. In adult patients, ligation is advised if access flow is above 1,000 mL/min, if cardiac risks are substantial and probability of renal graft loss is low.

• Regular management after renal transplant (6 months, a year, and yearly thereafter) is advised with of the AVF flow and echocardiographic studies.

• Access ligation is recommended for children with optimal renal transplant function and a patent elbow AVF who suffer from lowered distal tissue perfusion.
Chapter 9: Multiple Carcinomas in a Hemodialysis Induced Ischemic Hand of a Renal Transplant Patient

van Hoek F, Van Tits HW, Van Lijnschoten I, De Haas BD, Scheltinga MR,
(Transonic Systems Synopsis)

Case Report
Long-term use of immunosuppressants can cause squamous skin cell carcinoma (SCC), the most common skin cancer in transplant recipients.

In 2007, a 47-year old male, who had undergone kidney transplantation twice (1979, 1987) presented with several skin abnormalities on his head and left upper extremity as well as pain in all fingers of his left hand. His radiocephalic AVF (‘Cimino-Brescia’) was to remain patent for possible future use. Three hyperkeratotic lesions (two on his head and one on dorsum of his left hand) were eliminated and three well differentiated SCCs were detected.

During the next year, he developed seven additional manifestations of SCC (two on forehead and five in the left lower arm and hand region). Pathological examination of all seven SCCs from the lower arm and hand showed well differentiated carcinomas. The pain on left hand was progressive. Examination of his left hand demonstrated atrophy and intense coldness. A thrill was palpated over the well matured Cimino-Brescia AVF but radial arterial pulses were absent. His ischemic score was 184 indicating severe ischemia. AVF flow was 2,000 mL/min. HAIDI was indicated by photoplethysmography.

A banding surgical intervention was performed in an attempt to decrease access flow. Intraoperative AVF cramping nihilated access flow but finger pressure remained untracably low. Banding was aborted but a conservative treatment including attenuation of antihypertensive medication resulted in higher systolic pressure and subjectively decreased pain. He died in October 2008 due to complications following a cardiovascular operation.

Findings
• 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.

Reference
Chapter 10: Banding for High Flow Hemodialysis Access


Objective
To review High Flow Access (HFA) and to evaluate a surgical banding technique.

Overview Summary
This overview demonstrates that patients with a high flow access and cardiac overload benefit from surgical banding.

Incidence of HFA and associated cardiac failure is unknown but depends on definition, index of suspicion, and preferences of the multidisciplinary dialysis team. As nearly 5% of regular dialysis patients undergo surgery for Hemodialysis Access-Induced Distal Ischemia (HAIDI), it may be assumed that 2-4% of the patients may have HFA requiring correction.

Factors that contribute to the development of high flow once a hemodialysis access is constructed are largely unknown. According to a comparison study between HFA and HAIDI patient groups requiring operative correction, the HFA patient group underwent dialysis that was four times longer than the HAIDI patient group. The access location and type of anastomosis are other critical factors in determining onset and incidence of high flow.

For this review, access flows were routinely measured. Echocardiography was indicated if high access flow (>2 L/min) was repeatedly detected.

Clear criteria for treatment of HFA in the presence of cardiac failure have not been established. Non-surgical HFA management including treatment of anemia, electrolyte disturbance, and hypertension is heightened. The multidisciplinary team may choose to initiate invasive evaluation aimed at surgical HFA correction when signs of cardiac overload, HAIDI and a positive Nicoladoni-Branham sign continue while under optimal medical treatment. Surgical correction can be performed using a loco-regional anesthesia in day care. Monitoring of access flow and digital perfusion during surgery is mandatory. Ligation of large side-branches (basilica vein) may result in a significant reduction in access flow although associated digital ischemia is decreased. The surgical procedure may be terminated at this point. On the other hand, if ligation of side-branches do not substantially decrease access flow, or side-branches do not exist while most of the flow is shunted towards...
the axilla by a single route (cephalic vein), the banding may be carried out. Banding is the only clinically effective technique for HFA, if access flow is evaluated simultaneously during the operative procedure. Banding’s success depends completely on the use of intraoperative monitoring tools to guide the grade of the band’s constriction. Constriction of the banding is conducted by modifications in access flow and digital pressure. Timing of corrective surgery is controversial. If cardiac reserve is depleted following prolonged systemic overload, myocardial damage may have become irreversible.

Management of a patient dialysis access following successful kidney transplantation is debatable. Some recommend ligation while others argue that access closure may cause an intensive hypertension and intensified requirements of antihypertensive medication. No data which supports access ligation in patients with optimal kidney and cardiac function is found. Nevertheless, one may recommend ligation in case of HFA, left ventricular dilation, high risk for cardiac events or low probability of transplant loss.

No analyzed literature reported complications including infection, mycotic bleeding or aneurysms following banding for HFA. Banding does not accelerate venous intimal-medial hyperplasia. Immediate access occlusion after banding is rarely reported in patients operated for HFA (4%, 2/44). The only two patients whose banded access appeared occluded were operated without the guidance of intrapreoperative flow monitoring. High rates of clinical success and low incidence of access occlusion related with banding for HFA may appear to contrast with clinical data following banding for HAIDI.

Findings
- The present overview demonstrates that high access flow in an autogenous brachiocephalic upper arm direct access is associated with increased morbidity and possibly mortality.
- Size of the AV anastomosis was a major determinant for a surgical method to prevent development of a HFA following routine access creation.
- Some authors used a relatively small inflow artery to feed an upper arm access and did not observe high access flow.
- 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.
- The manifest discrepancy is explained in several ways:
  - The present overview displays that banding for HFA is almost always conducted using intraoperative flow control. On the other hand, several
studies on banding for HAIDI omitted to monitor access flow. As a result, bands may have been pulled too tight pushing access flow below its thrombotic threshold (<400 ml/min).

- In general flow in a HFA is significantly larger compared to flows in an access causing HAIDI. Accordingly, even after a considerable reduction in access flow following banding for HFA, residual flow may remain well above thrombotic levels. These findings provide a critical evidence that banding for HFA or HAIDI should always be performed under flow control, ideally combined with a technique reflecting digital perfusion (e.g. photoplethysmography)
Chapter 11: Summarizing Discussions, 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 (> 1month 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 overtime (‘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 HAID 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.
Chapter 11: Summarizing Discussions, Conclusions and Future Perspectives cont.

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.

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 cannot 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 side branches, 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 favorable, 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 1L/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’ Contribute 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 (P±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 loco regional
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 heterogeneity. 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 loco regional 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 AVE. In contrast, chronic HAIDI (>1 month after AVF insertion) is generally related to a maturing autogenous elbow AVE. 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 favorable 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 unfavorable, 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.
Chapter 11: Summarizing Discussions, Conclusions and Future Perspectives cont.

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 (alleged) 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’.
Chapter 11: Summarizing Discussions, Conclusions and Future Perspectives cont.

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 loco regional technique in an outpatient setting. In fact, the last three patients that received a banding procedure in the Maxima 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.

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Chapter 11: Summarizing Discussions, Conclusions and Future Perspectives cont.

Curriculum Vitae
Frank van Hoek

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 Maxima 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. JA van der Vliet).

All studies presented in the present thesis were performed in the Maxima 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).