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# Studies on high flow and hand ischaemia associated with an upper extremity haemodialysis access

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# Chapter 9

## Summarizing discussion and conclusions

## General

Wrist-based and elbow-based arteriovenous fistula (AVF) for haemodialysis (HD) were introduced the 1960's and 1970's, respectively.[1,2] Ever since, millions of people worldwide suffering from end-stage renal disease (ESRD) benefit from life-sustaining dialysis. While HD buys time, possibly in expectation of a renal transplant, this mode of renal replacement therapy (RRT) is not without long term sequelae. Apart from the fact that chronic intermittent HD is burdensome,[3] the arteriovenous access (AVA) itself may lead to long term complications limiting quality and duration of life. Two regularly occurring complications are development of a High Flow Access (HFA) and haemodialysis access-induced distal ischaemia (HAIDI). Earlier studies suggested that an elbow-based AVA imposes a greater risk of both of these complications as compared with wrist-based accesses.[4-6] As HD-population characteristics have changed over the last decades, with more people suffering from diabetes mellitus, peripheral arterial disease and hypertension while incident ESRD-patients are getting older, surgeons are forced to create more elbow-based instead of wrist-based accesses.[7] This trend is not without consequences with respect to HFA and HAIDI.

## Part I: High Flow Access (HFA)

The first part of this thesis (**Chapter 2-5**) focuses on the treatment and possible impact of high flow (Qa) on haemodialysis (HD) patients. An AVA access Qa between 400 and 600 mL/min usually suffices for adequate exchange of waste products in the artificial kidney.[8] In some cases, ongoing maturation drives Qa above 1500 mL/min and beyond. It should be realised that cardiac output in most adults ranges between 4000 - 5000 mL/min. An AVA may thus impose an increased workload on the cardiovascular system. It was earlier suggested that this additional burden possibly leads to a higher risk of high-output cardiac failure (HOCF).[9] Indeed, a Qa >2000 mL/min proved to greatly affect the cardiovascular system.[10]

A variety of interventions is available in order to correct an access with an excessive Qa. Banding is by far the oldest and commonest technique, relying on increased outflow resistance and thus resulting in a decreased Qa. An earlier study of our department in patients with a HFA demonstrated that the short-term efficacy of banding with respect to Qa reduction was disappointingly low as over half of all banded patients developed recurrent HFA within one year.[11] On the other hand, a technique termed

RUDI (revision using distal inflow) appeared more promising as just 16% developed a recurrence within in one year.[12] In **Chapter two**, three-year efficacy in terms of recurrence and patency was studied in 21 patients undergoing RUDI using a saphenous vein interposition graft. Interestingly, 70% remained free from recurrent high Qa within one year. However, 50% of patients did develop recurrent high flow (> 2 L/min) within the 3-year study period. Strikingly, not one patient with a HFA and concomitant HAIDI developed a recurrence. Three-year patency rates were acceptable but interventions to maintain patency (e.g., thrombectomy or percutaneous transluminal angioplasty) were frequently required. It was concluded that RUDI possibly performs better than banding on the short term, but more effective ways of long-lasting flow reduction have yet to be discovered. Future studies comparing different Qa reductive techniques are required.

The short term efficacy of Qa reduction of RUDI has been established in several publications. However, changes in arm vessel flow and diameter patterns following this procedure were unknown. Studying these phenomena may aid in understanding vessel functioning and unveil factors contributing to recurrent high Qa. In **Chapter three**, Duplex measurements during the first postoperative year in 15 patients undergoing RUDI using a greater saphenous vein (GSV) are reported. Brachial artery and GSV diameters remained constant whereas the diameter of the (inflow) radial artery proximal to the new anastomosis doubled. This increase was less profound in patients with HFA and concomitant HAIDI (+80%) compared with HFA patients without HAIDI (+130%). Furthermore, ulnar artery flow increased significantly, likely as compensation for an imminent loss in hand perfusion after the pressure drop in the distal radial artery. HFA recurrence may be looming as (dilated) brachial artery diameters did not change over time.

Most studies on the effects of high Qa on (cardiovascular) mortality are based on one or a few Qa-measurements. However, one might argue that it takes time to exhaust cardiac reserves with lethal consequences. **Chapter four** shows the results of a statistical joint-modelling approach studying the relation between cardiovascular death and flow incorporating all available Qa measurements (n=5408) in a population of 165 HD-patients during a 9-year time period. A <900 mL/min 'initial' (very first measurement once HD has started) Qa following maturation of a primary AVA was associated with an increased cardiovascular mortality risk (HR 4.05

[1.94-8.43]). A low initial Qa possibly reflects a suboptimal condition of the host's cardiovascular system at the time of access maturation. Qa increases over 3-month intervals were also associated with increased risk of cardiovascular death (HR 4.48/100 mL/3 months [1.44-13.97]). It was hypothesized that these Qa-increases over time reflect a progressively failing homeostasis in already frail HD-patients. Randomly timed (high) Qa values were not predictive of cardiovascular mortality. These findings may be considered in monitoring programs.

There is an ongoing debate on definition and management of a HFA. Some surgeons only perform Qa reduction when cardiac and/or hand ischaemic complaints have developed in the presence of a high Qa. Others advise reduction when Qa exceeds a certain threshold (e.g., 1500 or 2000 mL/min), independent of the presence of complaints. As there is a lack of consensus, **Chapter five** provides an overview of definitions of HFA and Qa reducing techniques that were proposed over the last 40 years. A total of 66 publications comprising 940 patients were identified. Interestingly, diabetes mellitus was more commonly present in patients with HFA and concomitant HAIDI (58%) compared with patients with HFA without HAIDI (18%). In comparison, diabetes mellitus rates in an average HD population are between 30-40%. All studied techniques were found to decrease Qa but degrees varied. For example, following banding, Qa dropped about 1.1 L/min (no guidance by intraoperative flow tool) to 1.4 L/min (with guidance of an intraoperative flow tool). After revision using distal inflow (RUDI), the decrease approximated 1.7 L/min. A great diversity in work-up, indication for surgery, thresholds, definitions of HFA and recurrence, follow-up and methods of Qa reduction was found precluding firm conclusions. Furthermore, the majority of studies was retrospective with a limited number of patients. Factors possibly aiding in the decision to operate, for example extremely high Qa, presence of cardiovascular disease or HAIDI, should play a role in decision making. Moreover, factors possibly contributing to a wait-and-see approach, e.g., short life expectancy, a single high Qa measurement or a wish for access ligation following stable renal transplant, were discussed.

## Part II: Haemodialysis access-induced distal ischaemia (HAIDI)

A brachial artery-based AVA usually offers an excellent mode for HD in terms of access patency and accessibility. In some patients however, the venous outflow segment may prove too short, too tortuous or too deep, precluding two needle dialysis. A basilic vein transposition (BVT), during which the basilic vein is rerouted more laterally along the biceps muscle, can help tackle this problem. It was observed that patients having symptoms of HAIDI prior to receiving a BVT reported a warmer and less painful hand following surgery. In **Chapter six**, results of a retrospective study in 10 patients with HAIDI undergoing BVT for an inadequate needle access segment were reported. Digital brachial indices (DBI, ratio of systolic finger pressure on systolic brachial-artery pressure; normal > 0.60) increased from 0.51 to 0.81 whereas scores of the hand ischaemic questionnaire dropped significantly from 220 to 9 (normal <50). Furthermore, a hypothesized inverse relation between DBI and questionnaire score was found. These findings indicated that BVT may effectively treat HAIDI-complaints. This effect is possibly explained by concurrent venous side branch ligation or construction of a smaller anastomosis thus attenuating the earlier 'pressure sink'.

In peripheral arterial occlusive disease (PAOD), presence of specific complaints and decreased toe pressures were found predictive of mortality.[13] In analogy to PAOD, HAIDI may in part also be considered a loco-regional expression of systemic vascular disease.[14] Intuitively, one may hypothesize that complaints and finger pressures in a patient with HAIDI are likely predictive of mortality. In **Chapter seven**, survival of 51 patients with different stages of HAIDI were compared with 48 peers without hand ischaemia. Patients with a severe type of HAIDI (e.g., unbearable pain during dialysis, rest pain, wounds; stage IIb to IV) were more likely to suffer from cardiovascular disease prior to the diagnosis HAIDI compared with patients with mild HAIDI (stage I to IIa) or no HAIDI at all. Intriguingly, low digital pressures -both with open as well as with compressed access-, high HAIDI complaint scores, and higher stages of HAIDI were related to increased mortality, even following correction for age and presence of cardiovascular disease and diabetes mellitus.

Old age, female sex, earlier AVA surgery and presence of diabetes mellitus are well-established risk factors for the development of HAIDI.[4,15] However, there is a need for additional parameters optimizing the preoperative counselling process prior to access construction. Historically, the Allen

test was performed to subjectively assess perfusion patterns of the hand in patients who were to receive a radial artery catheterisation or a wrist access, but with little success.[16] In **Chapter eight**, we determined in 105 patients whether an Allen test supported with digital plethysmography before access construction could predict the onset of HAIDI later on. Strikingly, all 10 patients who developed severe HAIDI requiring invasive measures displayed a radial or ulnar arterial dominance prior to access construction compared with about 60% of patients without HAIDI (total control group, n=95). The drop in digital pressure during the Allen test in the HAIDI-group was almost twice as high compared with controls (51 mmHg versus 27 mmHg). In addition, patients with a pressure drop ≥40 mmHg during an Allen test had a ten-times higher risk of developing HAIDI after access construction compared with patients with a drop <40 mmHg. These data suggest that patients who develop HAIDI have a diminished collateral hand perfusion reserve even before access construction. If additional risk factors for HAIDI are also present in such a patient, one may consider to opt for an alternative access type that is associated with a smaller chance of hand ischemia.

## Conclusions

1 Young age and high postoperative access flow (Qa) values following revision using distal inflow (RUDI) are predictive of high rates of recurrent HFA in hemodialysis (HD) patients.

2 HAIDI patients with a high flow access (HFA) have a smaller risk of recurrent high Qa following RUDI which is (partly) due to attenuated dilatation of the radial artery in this subgroup.

3 A low initial Qa as well as 3-months Qa-increases are predictive of a higher cardiovascular mortality risk, whereas single Qa values are of little relevance in HD patients.

4 Longitudinal Qa analyses are useful for predicting survival rates in HD populations.

5 Research on HFA and Qa reducing surgery for high Qa suffers from a lack of standardization in definition, indication for intervention and surgical techniques precluding definite conclusions on management.

6 Hand ischemia is abolished following a basilic vein transposition for an inadequate needle access segment.

7 Patients who developed severe HAIDI are at greater risk of untimely death compared to their counterparts with mild or no HAIDI.

8 Decreased finger pressures in HAIDI patients are predictive of overall mortality.

9 An Allen test complemented with finger plethysmography prior to construction of an arteriovenous access may identify patients who are at an increased risk of developing severe HAIDI later on.

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