



## Side Branch Ligation for Haemodialysis-access-induced Distal Ischaemia

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### WHAT THIS PAPER ADDS

- Chronic hand ischaemia is possibly caused by lowered distal perfusion pressure induced by a haemodialysis fistula. The role of open venous side branches close to the anastomosis of a brachial-artery-based Gracz fistula is unclear. This study suggests that side branch ligation may be beneficial in the treatment of hand ischaemia in patients with a brachiocephalic fistula using the Gracz technique.

### ARTICLE INFO

#### Article history:

Received 22 March 2012

Accepted 12 July 2012

Available online 3 August 2012

#### Keywords:

Haemodialysis

Haemodialysis access induced distal ischaemia

Side branch ligation

Digital pressure

### ABSTRACT

**Objective:** Chronic hand ischaemia is occasionally observed in haemodialysis patients with a brachiocephalic fistula using the Gracz technique. Open venous side branches of the access may contribute to lower peripheral perfusion pressures. This study reports on the effects of access side branch ligation (SBL) on ischaemia in patients with haemodialysis access induced distal ischaemia (HAIDI).

**Design, materials and methods:** Hand ischaemia was quantified using a published questionnaire (HIQ, minimal 0 points: no ischaemia, maximal 500: excruciating ischaemia). Finger pressures ( $P_{\text{dig}}$ , mmHg), digital brachial index (DBI) and access flow were measured before and after SBL.

**Results:** Twenty-two patients were operated for grade 2–4 HAIDI during 7 years, and 12 underwent SBL (as single procedure  $n = 5$ , preceding banding/DRIL  $n = 7$ ). Hand ischaemia was attenuated after SBL only ( $n = 5$ , HIQ  $216 \pm 39$  vs.  $73 \pm 26$ ,  $P = 0.04$ ). A 25% increase was observed in both  $P_{\text{dig}}$  ( $n = 12$ , before SBL:  $57 \pm 8$  mmHg, after:  $72 \pm 8$  mmHg,  $P = 0.012$ ) and DBI (before SBL:  $0.49 \pm 0.06$ , after:  $0.61 \pm 0.04$ ,  $P = 0.006$ ). Access flow did not change. All patients successfully resumed dialysis.

**Conclusion:** SBL may be effective as single or adjunctive surgical procedure in the treatment of HAIDI in the presence of a Gracz fistula.

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An autologous arteriovenous fistula (AVF) based at the brachial artery occasionally (4–9%) leads to progressive hand ischaemia (HAIDI, haemodialysis access induced distal ischaemia).<sup>1,2</sup> The ischaemia may be acute, subacute or chronic (<24 h, 1–30 days or > 1 month after AVF construction, respectively).<sup>2</sup> Chronic HAIDI is the most frequently occurring form, and this type is probably associated with continuing atherosclerosis of inflow arteries combined with a loss of blood pressure at the level of the arteriovenous anastomosis.<sup>2–4</sup> Moreover, ongoing dilation of venous portions of the AVF likely contributes to a progressive loss of locoregional blood pressure over time.<sup>2</sup> If patients have a brachial-

artery-based Gracz fistula, patent venous side branches may also contribute to an additional pressure loss.

Although an initial treatment regimen may be conservative, most HAIDI patients require an invasive procedure. If one accepts the premise that hand ischaemia is due to locoregional hypotension, a first step is arterial inflow visualisation aimed at identification of haemodynamically significant proximal stenotic disease. However, an inflow stenosis may be present in just a small number of patients with severe hand ischaemia.<sup>5,6</sup> If endovascular treatment of possible inflow stenosis does not alleviate ischaemic symptoms, most authors agree on instituting vascular surgery including distal revascularisation with interval ligation (DRIL), proximalisation of arterial inflow (PAI), revision using distal inflow (RUDI) or banding, depending on preoperative access flow.<sup>7–14</sup>

The role of patent venous side branches (SBs) of the AVF's outflow tract in the case of a brachial artery-based Gracz fistula in

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the aetiology of HAIDI is unclear. One may hypothesise that open SBs contribute to loss of arterial blood pressure due to shunting. As a consequence, open SBs may worsen distal ischaemia. As most SBs due to their deep position are unsuited for needling, ligation will usually not reduce dialysis capacity. A recent study on endovascular treatment of SBs in HAIDI reported encouraging results.<sup>15</sup> Data on open side branch ligation (SBL) as a treatment option for HAIDI are not available. Aim of the present study was to report on the results of SBL in patients with clinically significant hand ischaemia in the presence of an autologous brachial-artery-based AVF. We hypothesised that simple ligation of the access venous SBs would lead to attenuation of hand ischaemia with improved finger pressures.

## Materials and Methods

### Study population

The study was performed between January 2005 and February 2012 in the Maxima Medical Center (MMC), Veldhoven, The Netherlands. The MMC is an 850-bed hospital accommodating 400 000 patients in a semirural environment. A commonly used technique in this institution is the creation of a brachial-artery-based AVF termed a 'Gracz fistula'. The Gracz-type fistula entails mobilising of the median cubital vein or a deep perforating branch that is subsequently connected to the brachial artery. Using this technique, outflow is usually via both the upper arm cephalic and basilic vein.

Nearly 100 patients receive chronic haemodialysis on two locations of the MMC (Veldhoven and Eindhoven). Access flow is measured in duplicate every 2 months as suggested by KDOQI (Kidney Disease Outcomes Quality Initiative) using standard two-needle dilution techniques (HD01, Transonic Systems Inc, New York, USA). Detection and surgical treatment of haemodialysis vascular-access-related hand ischaemia is conducted using a standard protocol including intra-operative monitoring of access flow and finger pressures. By making an incision in the axillary region, access is gained to the main outflow vein used for measuring access flow. This is a standard part of our operative protocol but no extra incisions were required. Therefore, the local Medical Ethics Committee judged that approval for the present study was not required as this approach is considered standard care in our department.

Nephrologists and surgeons have a special interest in the management of hand ischaemia in the presence of an AVF. Most nurses are familiar with the symptoms of HAIDI. Patients who report symptoms possibly associated with ischaemia are discussed in a weekly multidisciplinary meeting. Patients are subsequently interviewed at the outpatient vascular department. A published questionnaire qualifying and quantifying hand ischaemia is used to score symptomatology (hand ischaemic questionnaire, HIQ).<sup>16</sup> This HIQ scores severity and frequency of five cardinal symptoms including pain, cramps, coldness, loss of strength and diminished sensibility. Ischaemic scores may range from 0 (no symptoms associated with ischaemia) to 500 (maximal symptoms).

A physical examination including hand inspection and radial artery palpation is performed. Reversibility of the ischaemia is determined using a fistula compression test. If a combination of the patient's history, physical examination and HIQ strongly suggests HAIDI, patients underwent finger plethysmography with and without fistula compression (Vasoguard Nicolet 8 MHz, Scimet, Bristol, UK). Both a <50 mmHg finger pressure ( $P_{dig}$ , in mmHg) or a <0.6 digital brachial index (DBI) are accepted cut-off points of hand ischaemia.<sup>17</sup> Patients were graded according to a published 1–4 scale analogous to the Fontaine classification (Table 1).<sup>2</sup> Invasive diagnostics were indicated if patients suffered from a grade 2b,

**Table 1**  
HAIDI classification.<sup>2</sup>

<b>HAIDI grade 1</b>	No clear symptoms but discrete signs of mild ischaemia 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.
<b>HAIDI grade 2a</b>	Complaints during dialysis sessions or intense use of the hand: <i>tolerable</i> pain, cramps, paresthesias, numbness or disturbing coldness in fingers or hand. Conservative treatment is indicated.
<b>HAIDI grade 2b</b>	Complaints during dialysis sessions or use of the hand: <i>intolerable</i> pain, cramps, paresthesias, numbness or disturbing coldness in fingers or hand. A combined treatment including conservative and invasive treatment (endovascular or surgical) is indicated.
<b>HAIDI grade 3</b>	Rest pain or motoric dysfunction of fingers or hand. Urgent invasive treatment supported by conservative measures is indicated.
<b>HAIDI grade 4a</b>	Limited tissue loss (ulceration, necrosis). Clinically significant hand function is probably maintained if ischaemia is reversed. Urgent invasive treatment supported by conservative measures is indicated.
<b>HAIDI grade 4b</b>	Irreversible tissue loss of the hand. Impossibility to preserve clinically significant hand function. Amputation is required.

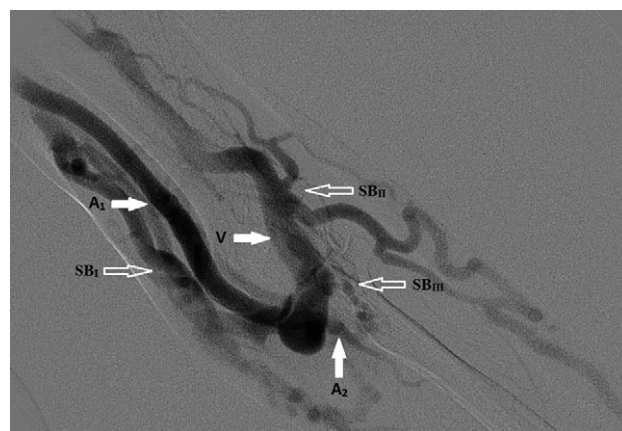
3 or 4 HAIDI. These patients underwent an angiography via the groin for identification and possibly optimisation of arterial inflow stenosis. The AVF's anastomosis and venous outflow tract including SBs were visualised (Fig. 1). If multidisciplinary agreement on an invasive strategy was attained, patients were informed on the nature of the operative procedure and verbally and in writing consented to its specifics. Patients qualified for the present trial if they:

1. harboured a brachial-artery-based AVF,
2. were suffering from at least a HAIDI grade 2b form and
3. angiography detected venous SBs in a 3–5 cm area in proximity to the anastomosis.

Patients were excluded if signs of impaired mental capacity or a language barrier were present.

### Operative protocol

Patients received general anaesthesia. Heart rate (HR, in beats/min), blood pressure (SBP, systolic blood pressure; DBP, diastolic blood pressure, mmHg) were obtained from the contralateral arm at regular



**Figure 1.** Angiographic view of a left sided Gracz fistula with a brachial inflow artery ( $A_1$ ) and a small radial artery ( $A_2$ ), a small basilic vein ( $SB_1$ ) and a distended cephalic outflow vein ( $V$ ) with two side branches ( $SB_{II}$  and  $SB_{III}$ ). Both side branches and the basilic vein were surgically ligated ( $SB_{I-III}$ ).

intervals via an on-line electrocardiogram (ECG) and a sphygmomanometer.  $P_{\text{dig}}$  of the index finger of the affected hand was serially determined using a plethysmographic technique under strict sterile conditions (VasoGuard Nicolet, 8 Mhz, Scimed Ltd, Bristol, UK).

Following sterile exposure of the entire arm, a longitudinal 2-cm incision downstream towards the axillary region was used to gain access to the main outflow vein (upper arm cephalic or basilic) as determined by the angiography. On-line access flow measurements were obtained using Optimax flow probes and ultrasonic transit time technique (HT 313, both Transonic Systems Inc, New York, USA). The arteriovenous anastomosis and neighbouring SBs as dictated by the angiography were dissected over a 3–5 cm area using the initial skin incision previously used for AVF creation. After a 1-min equilibration time period, access flow, HR, SBP, DBP and  $P_{\text{dig}}$  were measured. The dissected SBs were ligated (Fig. 2). All parameters were measured again 1 min after the last SB was ligated.

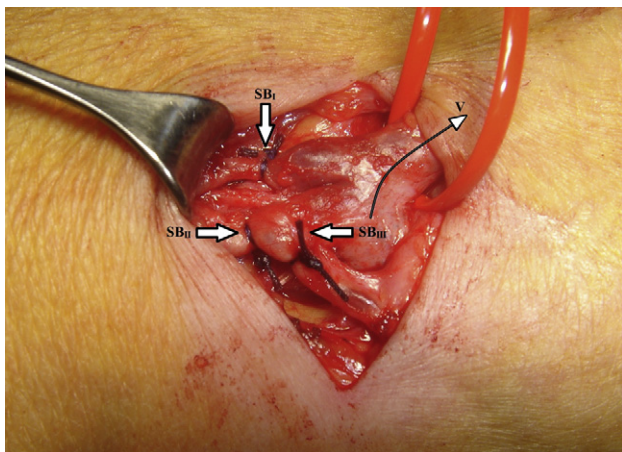
If  $P_{\text{dig}}$  and DBI did not increase above published cut-off points ( $P_{\text{dig}} > 50$  mmHg, DBI  $> 0.6$ ), patients additionally underwent banding (if access flow  $> 1$  L/min) or distal revascularization ( $< 1$  L min $^{-1}$ ). Patients were allowed dialysis on the same or next day if required by the blood results. Six weeks postoperatively, patients were evaluated for residual symptoms of hand ischaemia using the HIQ and a physical examination.

#### Definitions and analysis

Data recording and statistical analyses were performed using Statistical package for the Social Sciences (SPSS) version 17.0 (SPSS Inc., Chicago, IL, USA). Access flow just before SBL was set at 100%, and access flow values after SBL were expressed as a percentage thereof. These values were not expressed in absolute numbers as systemic blood pressure (and consequent arm blood flow) during general anaesthesia is considerably lower compared to values obtained during conscious states. A Wilcoxon-signed rank test was used to determine the effect of SBL on BP, HR,  $P_{\text{dig}}$  and DBI. All results were expressed as mean  $\pm$  standard error of the mean (SEM). A  $P < 0.05$  was considered significant.

#### Results

During the 7-year study period, a Gracx AVF was constructed in 140 patients. Of this population, 22 patients underwent revision for stage 2b–4 HAIDI. Angiography did not demonstrate significant stenoses in the inflow arteries in any patient ( $n = 22$ ). Twelve



**Figure 2.** Peroperative view of ligated side branches (SB<sub>I–III</sub>) in a Gracx fistula. The venous outflow tract (V) is marked with the long arrow, the brachial artery is not visible.

patients met all three inclusion criteria whereas 10 did not because they had no SBs within 3–5 cm of the anastomosis ( $n = 12$ , age  $69 \pm 5$  years, 5 female and 7 male, Table 2). None of these twelve patients included suffered from tissue loss (Table 2). Angiography demonstrated 1–3 possibly haemodynamically important SBs per study patient. A total of 25 SBs were ligated (basilic vein  $n = 10$ , other  $n = 15$ ). SBL as a single surgical treatment option was deemed sufficient (improved intraoperative  $P_{\text{dig}} > 50$  mmHg, DBI  $> 0.6$ ) in five patients. Just one of these five patients underwent a basilic vein ligation as a single therapeutic option only. The remaining seven individuals additionally underwent a second procedure during the very same operation as these two parameters were not improved sufficiently (banding  $n = 5$ , distal revascularisation using a venous bypass  $n = 1$ , basilic transposition  $n = 1$ ).

The time between AVF construction and revision for HAIDI was  $25 \pm 8$  months. SBL resulted in a higher  $P_{\text{dig}}$  in all patients ( $n = 12$ ,  $P_{\text{dig}}$   $57 \pm 8$  vs.  $72 \pm 8$  mmHg,  $P = 0.01$ ; DBI  $0.49 \pm 0.06$  vs.  $0.61 \pm 0.04$ ,  $P = 0.01$ , Fig. 3). Ligation had no effect on SBP or HR but DBP rose slightly ( $n = 12$ ,  $51 \pm 4$  to  $55 \pm 5$  mmHg,  $P = 0.04$ ). Intraoperative access flow did not change in the five patients undergoing SBL only ( $n = 5$ , 100% vs.  $99.6 \pm 0.4$ ,  $p = 0.600$ , Table 3).

All 12 patients underwent an uncomplicated dialysis session on either the same or the first postoperative day. Ischaemic symptoms obtained at the first outpatient control after 6 weeks were significantly attenuated in the patients receiving SBL as a single surgical procedure ( $n = 5$ , HIQ<sub>pre</sub>  $216 \pm 39$  vs. HIQ<sub>post</sub>  $73 \pm 26$ ,  $P = 0.043$ ). Postoperative access flows were not different compared to preoperative ones ( $n = 5$ , pre:  $600 \pm 160$  ml min $^{-1}$ , post:  $750 \pm 160$  ml min $^{-1}$ ,  $P = 0.27$ ). Ischaemic symptoms were also effectively treated in the remaining seven patients receiving both an SBL and an additional AVF revision, ( $n = 7$ , HIQ<sub>pre</sub>  $208 \pm 57$  vs. HIQ<sub>post</sub>  $45 \pm 29$ ,  $P = 0.043$ ) whereas access flows were decreased although not significant ( $n = 7$ , pre  $2215 \pm 488$  ml min $^{-1}$ , post:  $967 \pm 98$  ml min $^{-1}$ ,  $P = 0.12$ ). Postoperative tissue loss was not present in any of the 12 patients.

Perioperative complications associated with SBL were not observed. However, one patient developed an aneurysmal enlargement just proximal to the banding site leading to an occlusion 1 year after revision. A second patient developed a venous outflow stenosis leading to access occlusion after 18 months. Recurrent hand ischaemia or access occlusion were not observed, neither after SBL alone ( $n = 5$ , mean follow up  $38 \pm 14$  months) nor after a combined procedure ( $n = 7$ , mean follow up  $29 \pm 9$  months).

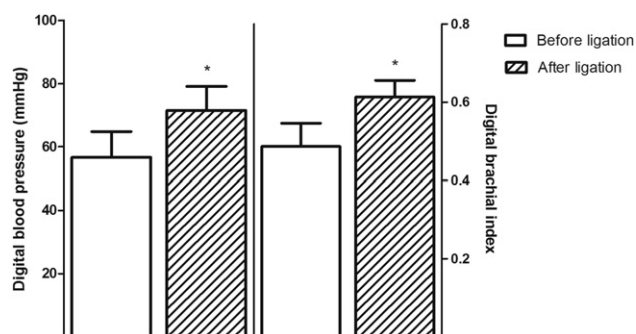
#### Discussion

SBL is incidentally indicated after a newly constructed AVF as a way of promoting maturation of the main outflow tract.<sup>18</sup> However, most venous portions of an AVF do not require SBL but demonstrate an overall dilatation over time as a response to arterial blood pressure (BP). If one accepts the premise that progressive hand ischaemia is due to a loss of arterial BP originating anywhere between heart and dialysis hand, therapy should focus on

**Table 2**

Demographics of patients with hand ischaemia undergoing elbow access side branch ligation.

N	12
Age (mean $\pm$ SEM)	$69 \pm 5$
Gender (male/female)	7/5
Diabetes Mellitus (yes/no)	1/11
Hypertension (yes/no)	8/4
Peripheral arterial occlusive disease (yes/no)	4/8
Coronary arterial disease (yes/no)	5/7
Brachial artery based AVF	12
Time after AVF construction (months)	$25 \pm 8$
Grade of HAIDI (2b/3/4)	8/4/0



**Figure 3.** Digital blood pressure (mmHg) and digital brachial index before and after side branch ligation in patients with hand ischemia ( $n = 12$ ,  $*p < 0.05$ ).

identifying that source of BP loss. If angiography excludes a stenotic subclavian, axillary or brachial artery, a BP decrease may in part be caused by the total venous outflow including main tract and its branches. As a consequence, ligating SBs with preservation of the main tract was hypothesised to attenuate BP loss. One earlier report incorporating five patients with hand ischaemia supports this hypothesis as symptoms were diminished following endovascular SB coiling.<sup>15</sup> The present study in 12 patients with signs of clinically relevant chronic HAIDI is the first to report on SBL as a single ( $n = 5$ ) or an adjunctive procedure ( $n = 7$ ), and the results strongly suggest the validity of this concept.

The initial diagnostic work-up in patients with suspected chronic HAIDI as presented in the current study, is non-invasive and straightforward. History is characteristic as most patients report typical symptoms of hand ischemia whereas physical examination aimed at identifying signs of hand ischaemia is simple. Radial artery pulsations are often absent or weak but may return after manual AVF compression.<sup>3,4</sup> However, if an AVF has several outflow tracts including basilic vein and/or distal cephalic vein, a compression test is probably less diagnostic as both the inflow artery and venous branches may accidentally be compressed. Lowered finger pressures ( $P_{\text{dig}} < 50$  mmHg) may increase after consecutively compressing these venous branches. Duplex analysis may identify significant flow in outflow veins including SBs. Ideally, a combination of plethysmography and Duplex may unveil the haemodynamic importance of SBs including the basilic vein.

A first invasive step in the management of patients with suspected chronic HAIDI is visualisation of the inflow arterial tree. Arterial inflow must be optimised prior to instituting open surgical procedures such as distal revascularisation. Some authors advise performing endovascular angioplasty even if the arterial inflow stenosis may seem limited.<sup>6,19,20</sup> Although an angioplasty of a 50% stenosis may be highly effective, this criterion is somewhat questionable.<sup>6,19–22</sup> It should be appreciated that the haemodynamic effect of just angiographically ‘minor’ stenoses may be substantial in a high-flow system as typically observed in a dialysis arm.<sup>3,5,23</sup> If a beneficial effect of angioplasty is doubted, intraluminal pressure measurements may quantify the haemodynamic effect of such a limited stenosis.<sup>24</sup> Interestingly, an inflow stenosis was not present in any of the 22 patients undergoing angiography in the 7-year study period in our institution. However, pressure measurements were not performed.

**Table 3**  
Haemodynamic effects of side branch ligation in patients with hand ischemia in the presence of an autologous elbow fistula.

	Before ligation	After ligation	P
Systolic BP (mmHg, $n = 12$ )	113 ± 8	116 ± 8	0.53
Diastolic BP (mmHg, $n = 12$ )	51 ± 1	55 ± 4	0.04
Heart rate (beats/sec, $n = 11$ )	61 ± 3	62 ± 3	0.62
Peroperative flow (% , $n = 7$ )	100	99.6 ± 0.4	0.60

If the arterial blood pressure loss is not due to stenotic inflow disease, a next step is the evaluation of the haemodynamic consequences of SBs during an endovascular or open surgical procedure. Several issues require addressing. The effect of any invasive procedure on finger perfusion should be monitored intra-operatively using plethysmography while ideally simultaneously measuring access flow.<sup>11,25</sup> The goal is to attain an increase in finger pressures while sufficient access flow for adequate haemodialysis is maintained. Another possible issue is the safety of a corrective AVF procedure. The systemic haemodynamic effects after manipulating a large flow AVF may be underestimated. For example, immediate cardiac death after AVF ligation has been reported, most probably due to acute intravascular overload.<sup>26</sup> Increased blood pressures are routinely observed after AVF occlusion.<sup>27</sup> The present study shows that SBL resulted in slightly higher DBP but SBPs and HRs remained unaltered. Access flow as measured in the outflow vein used for needling also did not change, resulting in an uncomplicated haemodialysis postoperatively in all patients.

What is the potential role of SBL in the therapeutic armamentarium for chronic HAIDI? Once surgery is indicated, any invasive procedure should be guided using intra-operative plethysmography and ideally access flow. If the diagnostic work up reveals SBs, these structures require dissection and ligation as a possible first step. If the  $P_{\text{dig}}$  (or DBI) is not pushed beyond the generally accepted cut-off point, one must continue with an additional (and more invasive) procedure such as PAI, DRIL, RUDI or banding. Conversely, these techniques may be less effective if haemodynamically important SBs are left untreated.

Can onset of a type of HAIDI that is exclusively due to patent SBs be prevented at the time of fistula creation? The present study included patients harbouring an AVF that was usually constructed between the brachial artery and the deep perforating elbow vein (Gracz).<sup>28</sup> It is unknown whether this type of AVF preferentially leads to HAIDI compared to other brachial-artery-based fistulas. In the Gracz type of AVF, outflow usually occurs via both the cephalic and the basilic upper arm vein. If basilic outflow appears dominant (compared to cephalic flow) according to a peroperative compression test, one may decide to ligate the basilic vein. By doing so, maturation of the cephalic pathway is stimulated whereas this type of SB HAIDI is prevented. However, it is currently unclear whether routine basilic vein ligation is necessary when the cephalic vein appears dominant on an intra-operative compression test. In our opinion, SBL at the time of fistula creation as a means to prevent hand ischaemia should not routinely be performed as the chances on successful maturation may be lowered.

In conclusion, open venous SBs of an autologous brachial-artery-based haemodialysis fistula, as in a Gracz fistula, may contribute significantly to chronic hand ischaemia. SBL may be considered as an adjunctive surgical procedure in the treatment of haemodialysis-access-induced hand ischaemia.

## Acknowledgements

All authors declare no competing interests, we have had no involvements that might raise the question of bias in the work reported or in the conclusions, implications or opinions stated.

In addition, Dr. Scheltinga is supported by a grant from the Stichting Hart – en Vaatziekten Zuid-Nederland (Heart and vascular disease foundation South – Netherlands).

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