**Supplementary Material**

**Pulse Wave Analysis and Pulse Wave Velocity for fistula assessment**

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**Supplementary Materials and Methods**

**Study enrollment and protocol**

In this prospective observational clinical pilot study, conducted from July 2012 until May 2013, local peripheral pulse wave analysis (PWA) was recorded ambilaterally in the A. brachialis as well as in the A. radialis and in addition approximately 1cm proximal of the anastomosis in the arterialized V. cephalic in forearms with arteriovenous fistula (AVF). Furthermore, pulse wave velocity (PWV) measurements were performed ambilaterally in three different segments located in the area of the cervical region and the upper limb, while duplex sonography was performed ambilaterally in the A. brachialis. Patients under 18 years, after heart transplantation, with acute infection or kidney failure, psychiatric disorders as well as pregnant or breast-feeding women were excluded. Peripheral PWA and PWV measurements were performed non-invasively in a triplicate by applanation tonometry using SphygmoCor® (AtCor Medical Pty. Ltd., West Ryde, NSW, Australia, Version 8.2 (1999-2008)), while duplex sonography was performed using Xario XG SSA-680 (Toshiba Medical Systems, Otawara, Tochigi, Japan). Patients were recruited at the department of Internal Medicine D of the University Hospital Münster in Germany. All investigations were performed by the same investigator. Prior to analysis, all patient data were anonymized and de-identified.

**Measuring points**

Local peripheral pulse waves (PWs) were recorded at the non-fistula arm of each patient, where the pulse of the A. brachialis (medial/ulnar in the antecubital fossa) and A. radialis (thumb side of the wrist joint) is palpable. At the patients’ fistula arm local peripheral PWA was performed at corresponding points of measurement proximal and distal of the fistula, i.e. where the pulse of the A. brachialis (medial/ulnar in the antecubital fossa, proximal of the radiocephalic fistula (RCF)) and A. radialis (thumb side of the wrist joint, distal of the RCF) is palpable (Figure 1). In addition, the pulsatile buzz of the arterialized V. cephalic was recorded approximately 1 cm proximal of the anastomosis, i.e. downstream in the arterialized superficial part of the venous drainage system (Figure 1). For local peripheral PWA all mandatory blood pressure measurements were restricted to the non-fistula arm to avoid AVF thrombosis. In order to assure the quality of each peripheral PW measurement done in this study, in general only PW measurements with an Operator-Index (given by SphygmoCor**®**) were accepted.

Ambilateral PWV measurements were performed between the above mentioned two points of measurement (A. brachialis and A. radialis) and each also in combination with the related side of the throat, where the pulse of the A. carotis is palpable. Again, all mandatory blood pressure measurements were restricted to the non-fistula arm to avoid AVF thrombosis. For quality control, only measurements with a measurement uncertainty (given by SphygmoCor**®**)of maximal were accepted.

Finally, duplex sonography was performed ambilaterally in the A. brachialis measuring standard parameters including flow, cross-section, different flow velocities, pulsatility index, resistance index, different diameters, and perimeter (for more details see Subsection *Analysed parameters*). In 4 patients a superficial brachial artery was detected at least at one arm. In this case, the flow and cross-section of both arteries (A. brachialis and A. brachialis superficialis) was measured independently and added up afterwards, all other parameters could not be quantified.

**Evaluation algorithm**

For data analysis we implemented a new algorithm in MATLAB® (Version: 7.14.0.739 (R2012a), The MathWorks Inc., Natick, MA, USA) computing seven different parameters (Figure 2) for each peripheral PW. We divided each peripheral PW into four consecutive sections (sections 1-4), using the characteristic points of a PW (namely the footpoint, first systolic maximum, dicrotic notch, first diastolic local maximum and footpoint of the following wave, see Figure 2). As a first step, we added three additional data points via linear interpolation between the raw data obtained from SphygmoCor® to increase the validity of the analysis. The registered peripheral PW is represented as a discrete map . A standard peripheral PW can be naturally divided at the global maximum, the subsequent local minimum (also known as “Dicrotic notch”, describes the border between systole and diastole), and the subsequent local maximum as shown in Figure 2. As a result of PW reflection, the global maximum of the registered PW can be slightly different from the global maximum of the PW without reflection. Therefore, we define the end of the first section at the time P\_T1 given by SphygmoCor®, which is defined as the maximum of the PW without wave reflection, and we denote this by . This phenomenon did almost not occur at the non-fistula arm but was found at the fistula arm in 43% of the patients (e.g. patient No. 10, see Figure 3a). The end of the second section, denoted by , for a standard PW can be defined as the subsequent local minimum of the curve, numerically computed as the subsequent zero of the first derivative of the PW (Supplementary Figures S1 and S2). This derivative of the discrete map is numerically computed using smoothing and forward difference quotients. In case there is no zero of the first derivative after , which mainly occurred for PWs registered at fistula arms, a manual analysis of the data revealed that it can be replacedby the first zero of the fourth derivative after the end of the first section and thus this will be the end of the second section (Supplementary Figures S1, S3 and S4). Similarly, the end of the third section, denoted by , is for a standard PW defined as the subsequent local maximum of the curve, numerically computed as the subsequent zero of the first derivative of the PW (Supplementary Figures S1 and S2). If this does not exist, it is defined as the first zero of the third derivative after the end of the second section (Supplementary Figures S1, S3 and S4). Finally, the end of the fourth section is defined as the end of the PW and denoted by . Our procedure to identify the end of the second and third section is in line with others (1;2).

For comparability a standardisation of the PW data was performed such that the total length of each analysed PW is 900ms. As the length of the systole (first two sections) is almost constant while the length of the diastole (last two sections) varies with the heart rate (3), this standardisation was performed separately for systole and diastole. By averaging over the registered times in the patients’ cohort the standardised lengths 340ms for the systole and 560ms for the diastole were fixed. Moreover, by the same method all PWs were standardised to a maximal value of 150mmHg to ensure comparability of PWs across varying levels of peak blood pressure values. We denote the standardised PW by .

**Analysed parameters**

The evaluation of ambilateral PWA was performed in a structured manner as a comparison of corresponding sections of the PWs (1–4) at the different points of measurement in the non-fistula and fistula arms. The slope in [] in each section can be computed with the following formula letting

where denote the standardised times at the end of each section. This results in 4 parameters in [] defined as differences between the arithmetically averaged slope between corresponding sections of the non-fistula and fistula arm at each point of measurement ( radial, brachial). More formally, , where and denote the averaged slope at the non-fistula ( non-shunt) and fistula ( shunt) arm respectively. Analogously, we define the parameters for measurements in the arterialized V. cephalic ( close to anastomosis) and in comparison to the average slopes at the non-fistula and fistula arm respectively. The sum of the slope differences, the variable (in []), was defined as at each point of measurement ( radial, brachial). Here was subtracted as its mean value was negative as opposed to the other variables.

As peripheral PWs are represented as discrete maps, the area under the curve in [] can be computed using the following formula

for , where for denote the standardised times at which the peripheral PW was recorded or linearly interpolated. This results in 3 parameters in [] defined as differences between the arithmetically averaged areas between corresponding parts of the curve (systolic, diastolic, and total area under the curve, corresponding to the tuples and above) of the non-fistula and fistula arm at each point of measurement ( radial, brachial). More formally, , where and denote the average area at the non-fistula ( non-shunt) and fistula ( shunt) arm respectively. Analogously, we define the parameters for measurements in the arterialized V. cephalic ( close to anastomosis) and in comparison to the average areas at the non-fistula and fistula arm respectively.

The parameters regarding the PWV in [] are defined as differences between the arithmetically averaged PWV of three measurements between corresponding segments of the cervical region and the upper limb ( carotid-radial, carotid-brachial, brachial-radial) of the non-fistula ( non-shunt) and fistula ( shunt) arm.

The duplex sonographic parameters are defined as differences between measured parameters in the A. brachialis of the non-fistula ( non-shunt) and fistula ( shunt) arm. The following parameters were considered: Difference of flow in [], cross-sectionally averaged flow in [, maximal, minimal, and enddiastolic flow velocity in [] for , average flow velocity in [], systolic-diastolic ratio , pulsatility index , resistance index , cross-section in [], perimeter in [] and horizontal and vertical diameter in [] for . The flow rate was computed by the ultrasound device by multiplying the timely averaged flow velocity with the cross-section , neglecting the reducing flow towards the vessel wall and hence overestimating the fistula flow. Therefore, the cross-sectionally averaged flow was used as the sonographic estimate of the fistula flow. It was calculated as according to (4).

**References**

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