

## --- DATA SUPPLEMENT ---

### **Measure of wave intensity as non-invasive surrogate for cardiac function predicts mortality in hemodialysis patients**

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**Table S1: Baseline characteristics of patients from the ISAR and the NGHN cohort separately.**

Characteristic	NGHN	ISAR	All
N	214	344	558
Age (yr)	62.5 [52,74]	69 [55,77]	66 [53,76]
Sex-male, n (%)	139 (65 %)	234 (68 %)	373 (67 %)
Body mass index (kg/m <sup>2</sup> )	25.7 [23.2,29.5]	25.2 [22.8,28.7]	25.4 [22.9,28.9]
Dialysis vintage (mo)	28.0 [12.0,59.0]	41.1 [22.7,76.6]	35.5 [17.3,70.5]
Effective time of dialysis (h)	4.0 [4.0,4.0]	4.23 [4.0,4.5]	4.02 [4.0,4.38]
UFV (ml)	2057 (1003 SD)	2220 (1127 SD)	2158 (1083 SD)
UF rate (ml/h)	527 (263 SD)	501 (248 SD)	511 (254 SD)
Serum albumin (g/l)	40.2 (3.72 SD)	39.9 (4.14 SD)	40 (3.99 SD)
Presence of diabetes, n (%)	63 (29 %)	135 (39 %)	198 (35 %)
History of hypertension*, n (%)	196 (92 %)	326 (95 %)	522 (94 %)
Use of statin, n (%)	94 (44 %)	136 (40 %)	230 (41 %)
Use of anticoagulation med, n (%)	131 (61 %)	52 (15 %)	183 (33 %)
Use of antihypertensive med, n (%)	179 (84 %)	314 (91 %)	493 (88 %)
SBP (mmHg)	130 (18.1 SD)	123 (17 SD)	126 (17.8 SD)
DBP (mmHg)	78.5 (12 SD)	72.4 (11.8 SD)	74.8 (12.2 SD)
PP (mmHg)	50.6 [42.8,60]	48.7 [41.2,56.5]	49 [41.6,57.7]
Heart rate (1/min)	73.2 (8.99 SD)	71.5 (10 SD)	72.2 (9.67 SD)
SDR (-)	2.43 [2.07,2.77]	2.51 [2.16,3.01]	2.48 [2.12,2.92]
All-cause mortality, n (%)	78 (36 %)	115 (33 %)	193 (35 %)
CV mortality, n (%)	45 (21 %)	47 (14 %)	92 (16 %)

Results are presented as mean (standard deviation) and median [inter-quartile range] for normally and non-normally distributed data, respectively; categorical data as total number (percentage).

Abbreviations: UF, ultrafiltration; UFV, ultrafiltration volume; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; SDR, S to D ratio from wave intensity analysis; AF, atrial fibrillation; HF, heart failure; CV, cardiovascular. \*History of hypertension was defined as either use of antihypertensive medication and/or 24h blood pressure >140/90 mmHg.

**Table S2: Baseline characteristics of excluded and included patients of pre-/early- and post-dialytic analysis.**

<b>Characteristic</b>	<b>Pre-/Early- and /Post-dialytic Subgroup</b>	<b>Excluded</b>	<b>All</b>
N	438	120	558
Age (yr)	65 [52,75]	69 [58,77]	66 [53,76]
Sex-male, n (%)	282 (64 %)	91 (76 %)	373 (67 %)
Body mass index (kg/m <sup>2</sup> )	25.5 [23,29.3]	25 [22.6,28.1]	25.4 [22.9,28.9]
Dialysis vintage (mo)	33.4 [16.4,67]	47.2 [23.7,79.6]	35.5 [17.3,70.5]
Effective time of dialysis (h)	4.00 [4.00,4.37]	4.17 [4.00,4.43]	4.02 [4.00,4.38]
UFV (ml)	2151 (1088 SD)	2180 (1070 SD)	2158 (1083 SD)
UF rate (ml/h)	512 (256 SD)	510 (248 SD)	511 (254 SD)
Serum albumin (g/l)	40.0 [38.0,42.3]	39.6 [37.9,42.0]	40.0 [38.0,42.2]
Presence of diabetes, n (%)	159 (36 %)	39 (33 %)	198 (35 %)
History of hypertension*, n (%)	410 (94 %)	112 (93 %)	522 (94 %)
Use of statin, n (%)	184 (42 %)	46 (38 %)	230 (41 %)
Use of anticoagulation med, n (%)	155 (35 %)	28 (23 %)	183 (33 %)
Use of antihypertensive med, n (%)	388 (89 %)	105 (88 %)	493 (88 %)
SBP (mmHg)	132 [119,145]	129 [114,146]	132 [119,145]
DBP (mmHg)	80.8 (13.9 SD)	80.7 (15.6 SD)	80.8 (14 SD)
PP (mmHg)	50.5 [42.4,60.8]	50.8 [43.5,63.1]	50.5 [42.5,60.8]
Heart rate (1/min)	71.7 (10.6 SD)	74.7 (13.6 SD)	71.9 (10.9 SD)
SDR (-)	2.48 [2.12,2.88]	2.46 [2.11,3.04]	2.48 [2.12,2.92]
All-cause mortality, n (%)	150 (34 %)	43 (36 %)	193 (35 %)
CV mortality, n (%)	71 (16 %)	21 (18 %)	92 (16 %)

Results are presented as mean (standard deviation) and median [inter-quartile range] for normally and non-normally distributed data, respectively; categorical data as total number (percentage).

Abbreviations: UF, ultrafiltration; UFV, ultrafiltration volume; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; SDR, S to D ratio from wave intensity analysis; AF, atrial fibrillation; HF, heart failure; CV, cardiovascular. \*History of hypertension was defined as either use of antihypertensive medication and/or 24h blood pressure >140/90 mmHg.

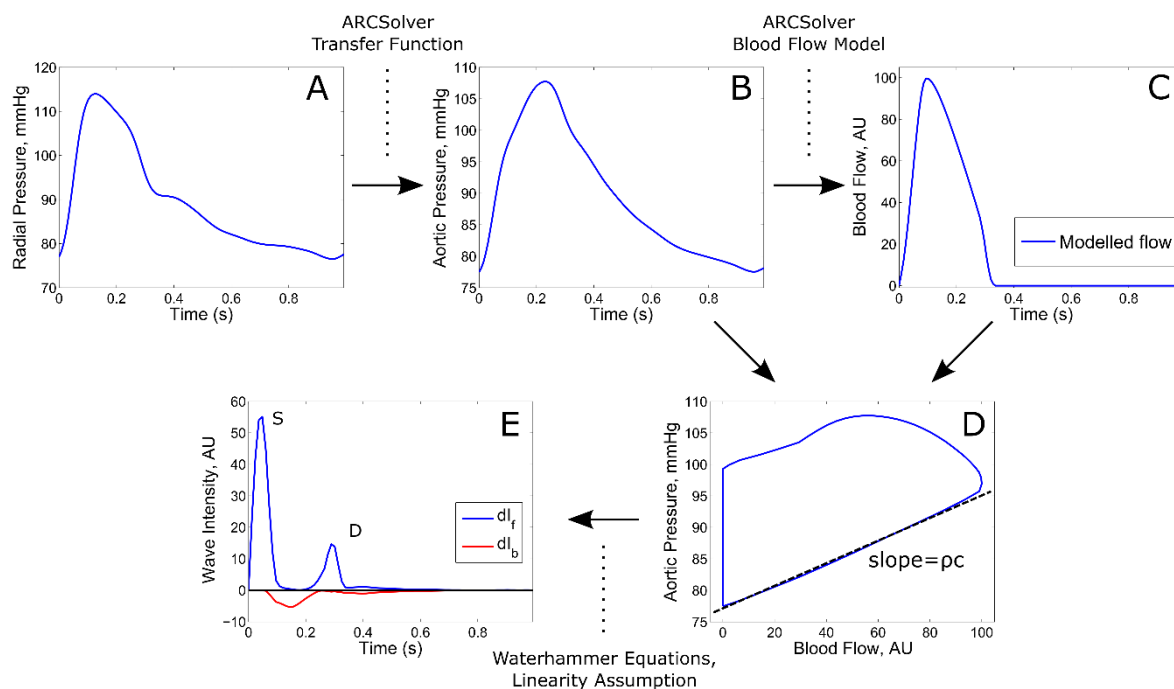
**Table S3: Reasons for cardiovascular death**

In the table, the reasons for cardiovascular death are presented for the whole study population and the two dedicated groups based on atrial fibrillation and heart failure.

<b>Reasons</b>	<b>AForHF (N=196)</b>	<b>noAForHF (N=362)</b>	<b>All (N=558)</b>
Sudden cardiac death	31	23	54
Myocardial infarction	3	6	9
Heart failure	7	4	11
Major stroke	3	3	6
Cardiac surgical procedure	0	2	2
Pulmonary embolism	1	1	2
Other cardiovascular reasons	3	5	8
Number of cardiovascular deaths	48	44	92

Abbreviations: AF, atrial fibrillation; HF, heart failure.

**Figure S4: Detailed description and visualization for calculation of SDR** (updated and based on own prior work [1]): Brachial pulse waveforms were obtained with the oscillometric Mobil-O-Graph 24-hour PWA device (A) and transformed to the aortic pressure  $P$  using the validated ARCSolver Transfer Function (B). Aortic blood flow  $Q$  was then determined by combining a Windkessel model relating pressure and flow with a minimal work criterion using the ARCSolver® algorithms (AIT Austrian Institute of Technology GmbH, Vienna, Austria) as described in [2] (C). Aortic blood flow was subsequently used as an estimate of flow velocity  $U$  [3]. Since PU-loop during early systole is approximately linear, pulse wave velocity  $c$  times blood density  $\rho$ , which reflects the blood density ( $1050 \text{ kg/m}^3$ ) is estimated from the slope (D). Consequently, changes in pressure ( $dP$ ) and flow velocity ( $dU$ ) were computed and separated into forward and backward travelling components using the Waterhammer equations  $dP_{f,b} = \pm \rho c dU_{f,b}$  and a linearity assumption  $dP = dP_f + dP_b$  and  $dU = dU_f + dU_b$  [1,4], where  $dP$  and  $dQ$  denote changes per time step and subscripts  $f$  and  $b$  denote forward and backward travelling components, respectively. Finally, forward and backward wave intensities are defined as the product of changes in pressure and flow velocity as  $dI_{f,b} = dP_{f,b} * dU_{f,b}$ , see E [1,5]. Forward wave intensity is characterized by two dominant peaks, called S and D.



- [1] Hametner B, Parragh S, Weber T, Wassertheurer S. Wave intensity of aortic root pressure as diagnostic marker of left ventricular systolic dysfunction. *PLoS One*. 2017;12(6):e0179938. doi: 10.1371/journal.pone.0179938.
- [2] Hametner B, Wassertheurer S, Kropf J, Mayer C, Holzinger A, Eber B, Weber T. Wave reflection quantification based on pressure waveforms alone--methods, comparison, and clinical covariates. *Comput Methods Programs Biomed*. 2013;109(3):250-9. doi: 10.1016/j.cmpb.2012.10.005.

- [3] Hametner B, Wassertheurer S, Kropf J, Mayer C, Holzinger A, Eber B, et al. Wave reflection quantification based on pressure waveforms alone-Methods, comparison, and clinical covariates. *Comput Meth Programs Biomed* 2013; 109(3):250–9.
- [4] Parker K, Jones C. Forward and backward running waves in the arteries: analysis using the method of characteristics. *J Biomech Eng* 1990; 112(3):322–6.
- [5] Mynard JP, Kondiboyina A, Kowalski R, Cheung MMH, Smolich JJ. Measurement, Analysis and Interpretation of Pressure/Flow Waves in Blood Vessels. *Front Physiol.* 2020 Aug 27;11:1085. doi: 10.3389/fphys.2020.01085.