Universitätsspital Zürich

Klinik für Angiologie

Direktorin: Prof. Dr. med. B. Amann-Vesti

Arbeit unter Leitung von PD Dr. med. M. Husmann

Severity of Peripheral Arterial Disease is Associated with Aortic Pressure Augmentation

INAUGURAL-DISSERTATION

zur Erlangung der Doktorwürde der Medizinischen Fakultät

der Universität Zürich

vorgelegt von

Kathrin Mosimann Fennema

von Lauperswil, Bern

Genehmigt auf Antrag von Prof. Dr. med. B. Amann-Vesti

Zürich 2011

TABLE OF CONTENTS

ABSTRACT 3

INTRODUCTION 4

METHODS 5

RESULTS 7

DISCUSSION 8

REFERENCES 10

LEGENDS 13

ACKNOWLEDGEMENTS 19

CURRICULUM VITAE 20

ABSTRACT

Background: Peripheral arterial disease (PAD) is associated with increased cardiovascular mortality that correlates with peripheral perfusion impairment as assessed by the ankle-brachial arterial pressure index (ABI). PAD leads to arterial stiffness and increased pulse wave velocity that might impact central aortic pressures and subendocardial perfusion during diastole.

Aim: To investigate whether ABI impairment correlates with the aortic augmentation index (AIx), a measure of pulse wave velocity and reflection, and the subendocardial viability ratio (SEVR).

Patients and Methods: AIx and SEVR were assessed by radial applanation tonometry in 65 patients with stable PAD (Rutherford stage I-III) at a tertiary referral center. AIx (corrected for heart rate) and SEVR were tested in univariate and multivariate linear regression models to determine the association with ABI.

Results: Mean values were ABI 0.8 ± 0.2, AIx 31 ± 7%, and SEVR 141 ± 26%. Multiple linear regression with AIx as the dependent variable revealed a significant negative association with ABI (β = -11.5 [95% confidence interval (CI), -18.6 to -4.5], p = 0.002). Other variables associated with AIx included diastolic blood pressure (β = 0.2 [95% CI, 0.1 to 0.4], p < 0.001), height (β = -46.2 [95% CI, -62.9 to -29.4], p < 0.001), body mass index (β = -0.4 [95% CI, -0.8 to -0.1], p = 0.023), and smoking (β = 3.6 [95% CI, 0.6 to 6.6], p = 0.019). Multiple regression with SEVR as the dependent variable showed a significant correlation with ABI (β =33.2 [95% CI, 2.3 to 64.1], p = 0.036).

Conclusion: Severity of lower limb perfusion impairment is related to central aortic pressure augmentation and to SEVR. This may be a pathophysiologic mechanism that impacts cardiac prognosis in patients with PAD.

INTRODUCTION

Peripheral arterial disease (PAD) is a common manifestation of atherosclerosis affecting more than 5% of the aged population [1-2]. Despite having a relatively low rate of peripheral complications and limb amputations, PAD is associated with impairment in functional activity and an increased risk of cardiovascular events [3-4]. For this reason, PAD is considered a marker for systemic atherosclerosis [5]. To date, the most powerful prognostic indicator in PAD patients is the ankle-brachial pressure index (ABI) [6-8]. ABI is used to measure impairment of lower limb perfusion and has been shown to predict survival rate in patients with PAD [1, 9-10].

The mechanisms through which the presence of PAD increases the risk of cardiovascular events are not understood in detail. PAD represents a vascular disease with extensive atherosclerotic involvement. This is paralleled by systemic inflammation and increased level of oxidative stress, both are known to destabilize atherosclerotic plaque and may thus be associated with vascular events [11]. In addition, the extensive atherosclerotic alterations along the vascular tree conduit are thought to increase pulse wave velocity and lower limb arterial obstructions may favor premature pulse wave reflections [12-13].

Pulse wave analysis conducted using radial tonometry has been shown to correlate with both invasively measured central aortic pressure and subendocardial perfusion, and has been applied to investigate arterial stiffness in different diseases [14].

Khalegi et al have reported that pathological ABI was independently associated with increased central aortic pressure augmentation[12]. Whether the degree of ABI impairment is linked to elevated central aortic pressures and decreased subendocardial viability ratio (SEVR) is not known to date.

We hypothesize that the degree of ABI impairment is related to increased central aortic augmentation index (AIx) and decreased SEVR and therefore assessed these surrogate markers non-invasively by radial pulse wave analysis in patients with stable PAD.

METHODS

Patients

This prospective, single-centre evaluation assessing ABI and pulse wave analysis in consecutive patients with PAD was conducted at a tertiary referral centre. Only patients with chronic and stable PAD were eligible for the study. Exclusion criteria were critical limb ischemia (Rutherford IV-VI), cardiac arrhythmia, and chronic inflammatory vascular disorders. Patients with incompressible tibial and peroneal arteries due to mediacalcinosis were excluded. Patients were not withdrawn from regular medication. The local ethics committee approved the study (Nr. 1741/2009) and all patients provided written informed consent. The study was conducted according to Good Clinical Practice standards. The following data were collected: medical history, peripheral systolic and diastolic blood pressures, body mass index, vascular risk factors (arterial hypertension, diabetes mellitus, dyslipidemia, smoking), comorbidities and medication, ABI, and pulse wave analysis.

Ankle-brachial arterial pressure index assessment

ABI assessment was performed as part of the standard diagnostic procedure. Brachial systolic and diastolic blood pressures on both arms with traditional cuff manometry were measured in triplicate according to the Riva Rocci method. Systolic ankle blood pressures of the posterior tibial artery, anterior tibial artery, and peroneal artery on both legs were obtained by hand-held 6 MHz Doppler probe (Kranzbühler, Logidop 2, Pilger Medical Electronics, Switzerland). For both legs, ABI was calculated as the ratio of the highest ankle pressure divided by the highest brachial systolic blood pressure. The lower ABI value was chosen as study parameter, because of its higher correlation with PAD severity.

Radial artery pulse wave analysis

Applanation tonometry of the radial artery was performed with the SphygmoCor system (AtCor Medical, Sydney, Australia) by a single observer, with patients in the supine position to acquire radial artery waveforms [15]. A validated transfer function was used to generate the corresponding ascending aortic pressure waveform. Augmented pressure was defined as the difference between the second and the first systolic peak, and AIx was expressed as a percentage of the pulse pressure (difference between systolic and diastolic pressure) [16]. AIx was corrected for heart rate of 75 per minute (AIx@HR75). Subendocardial blood supply as a parameter evaluating the risk of myocardial ischemia was expressed with the SEVR, the ratio of the diastolic phase (diastolic time index) to that of the systolic phase (time tension index) as measured by the SphygmoCor.

Statistical analysis

Descriptive statistics for continuous variables are given as mean ± standard deviation. For categorical variables, results are presented as a frequency and a percentage. ABI was considered as an independent variable, and AIx and SEVR as dependent variables. We examined univariate and multivariate linear regression models to determine the association between ABI and the augmentation index (AIx@HR75) and SEVR. The following covariates were used in the multivariate models: age, sex, systolic and diastolic blood pressure, height, body mass index, cardiovascular risk factors (hypertension, smoking history, diabetes mellitus, and dyslipidemia), comorbidities (coronary artery disease, cerebrovascular disease, renal insufficiency), and use of antihypertensive medication. All continuous variables were centered at their respective means. Categorical variables were dichotomized as present or absent. Comorbidities were dichotomized and marked as present in subjects with either prevalent cardiovascular or cerebrovascular disease, or renal insufficiency. Similarly, medication was dichotomized and categorized as present in case a subject was under current treatment with an angiotensin converting enzyme-inhibitor, an angiotensin-II-receptor inhibitor, a calcium-antagonist, or nitrates. We included interaction terms between all covariates in the model and the ABI. Interaction was graphically inspected in addition to a chunk-wise statistical assessment using the multiple-partial F-test to compare the unrestricted and restricted model. Next, a chunk-wise elimination of non-significant main effects was performed. Robustness of the modelling strategy was verified by using other modelling strategies (stepwise backward and forward procedures). Values of 2-sided $p < 0.05$ were considered statistically significant. All analyses were performed with Stata 11.1 for Windows (StataCorp LP, College Station, TX).

RESULTS

The characteristics of the study population are summarized in table 1.

Graphical as well as statistical examination did not indicate any relevant interaction between the candidate covariates and the two independent variables of interest ($p = 0.186$ for the model assessing AIx@HR75, and $p = 0.576$ for the model assessing SEVR).

Data on ABI, heart rate, and pressure characteristics, as well values for AIx and SEVR, are provided in table 2.

When using a univariate linear regression, AIx was significantly associated with ABI with a coefficient of -13.0 (95% confidence interval [CI], -21.6 to -4.4; $p = 0.004$). All covariates except diastolic blood pressure, history of smoking, height, and body mass index were removed from the model in backward multiple linear regression elimination with AIx@HR75 as the dependent variable (table 3). The multiple-partial F-test between the unrestricted model and the final model indicated a significance of 0.351. Total variance of AIx@HR75 explained by the final model was 51%. The selection of variables included into the model was confirmed by the stepwise selection procedures. The partial regression plot for AIx@HR75 and ABI are shown in figure 1 and indicated that the lower the ABI, the higher AIx@HR75.

Likewise, univariate linear regression revealed a statistically significant association between SEVR and ABI, with a coefficient of 54.0 (95% CI, 22.0 to 86.0; $p = 0.001$). In the multiple linear regression model, the β for the ABI was 33 (95% CI, 2.3 – 64.1; $p = 0.036$). Significance from the multiple-partial F-test between the unrestricted model and the final model was 0.657. The model indicated a 0.35 variance of SVER. The partial regression plot for SEVR and ABI are shown in figure 2 and exhibited a positive correlation between ABI and SEVR. Stepwise procedures again confirmed variable selection in the model.

DISCUSSION

The main finding of this study is that the severity of PAD—as assessed by ankle-brachial arterial pressure index—is independently associated with central aortic pressure augmentation and SEVR. This indicates that the impairment of peripheral arterial perfusion has a negative effect on systolic and diastolic cardiac function. Although epidemiological studies have shown that ABI is a powerful prognostic parameter for survival in PAD patients, the distinct pathophysiologic mechanism is still not fully understood [1, 17].

Only limited data exist on AIx in patients with peripheral arterial disease [12-13, 18]. By examining 457 adults without history of coronary artery or cerebrovascular disease, Khalegi et al reported that AIx@HR75 is independently associated with a pathological ABI [12]. In our study we have additionally demonstrated that the severity of lower limb arterial perfusion inversely correlates with AIx@HR75. Khalegi et al used the ABI as the variable of interest (dependent) and reported an association with AIx@HR75, older age, shorter height, female sex, and anti-hypertensive medication. In our model using AIx as the variable of interest and investigating only subjects with PAD, we found a significant association with ABI, height, body mass index, smoking, and diastolic blood pressure. Similarly, Amoh-Tonto et al reported that patients with coronary artery disease and ABI below 0.94 had higher AIx than those with normal ABI.

In addition to the evaluation of central aortic pressure augmentation, pulse wave analysis allows for the assessment of SEVR [19-20]. The ratio of the diastolic (diastolic time index) to the systolic phase (time tension index) in the central aortic profile has a close correlation with the blood supply to the subendocardium [20-21]. Hence, SVER derived from aortic pulse waveforms is a non-invasive estimation of subendocardial blood supply. Saito et al found that AIx and pulse pressure (systolic-diastolic pressure amplitude) are independent predictors for lower coronary flow reserve [22]. In our study, the model of multivariate regression analysis with SEVR as the dependent variable shows that there is a significant association between ABI and systolic and diastolic peripheral blood pressures. In addition to the inverse correlation between ABI and AIx, our findings suggest that PAD is associated with elevated central aortic pressure and decreased subendocardial blood supply, which indicates that the degree of peripheral perfusion impairment may affect subendocardial perfusion.

In order to understand this potential pathophysiologic context in PAD, the physiology of pulse wave propagation and reflection need to be reviewed. PAD impairs arterial compliance due to atherosclerotic arterial wall changes, resulting in increased arterial wall stiffness along the vascular conduit with a poorer distal run-off. This is thought to lead to a central systolic pressure augmentation and decreased central diastolic pressure through a) increased pulse wave velocity, given that pulse wave propagation is accelerated by elevated arterial stiffness, and b) premature pulse wave reflections at atherosclerotic bifurcations and obstructions [23-25]. The extent of arterial stiffness and the number and pattern of arteries and arterioles of the distal run-off are important determinants of the timing and amplitude of the arterial wave reflection [26]. Premature arterial wave reflection impacts on cardiovascular risk because elevated AIx has been reported to be associated with coronary artery disease and cardiovascular events [27-29]. These hemodynamic changes in the central aorta unfavourably affect heart function by increasing cardiac afterload

(central systolic pressure augmentation) and may decrease myocardial perfusion due to a lower pressure during diastole [22]. Buckberg et al have demonstrated that the ratio of the area of the diastolic phase (diastolic pressure time index) to that of the systolic phase (time tension index) in the central aortic profile has a close correlation with the blood supply to the subendocardium [30-31].

Elevated AIx and lower SEVR may cause acceleration of coronary artery disease and render atherosclerotic plaque more vulnerable due to a possibly impaired coronary blood flow during diastole [22]. Further studies on this pathophysiologic mechanism are needed to prove these findings. The assessment of AIx and SEVR can thus be considered easily accessible surrogate parameters of cardiovascular risk and might be used to study the effect of different treatment options as well as lifestyle modification in patients with PAD. It nevertheless remains uncertain whether the assessment of AIx and SEVR provides more powerful information concerning the cardiovascular prognosis of these high-risk patients than the measurement of ABI. Moreover, the present analysis is based on a cross-sectional study design investigating a small population with PAD. Therefore, other factors that might contribute to the correlation between ABI and cardiovascular prognosis are eventually not identified, since multilevel vascular involvement, inflammation, and decreased physical activity are potential cofactors influencing the prognosis. A reduction in physical activity has been shown to correlate with increased cardiovascular morbidity. Interestingly, two independent groups have recently reported that pulse wave velocity is associated with walking distance even after adjustment for ABI in patients with PAD (n=75 and n= 106) [13, 32].

In conclusion, AIx and SEVR are related to ankle-brachial arterial pressure index in patients with PAD independent of age, comorbidity, and medication. This indicates a strong association between peripheral arterial perfusion impairment and central aortic and cardiac function.

REFERENCES

1. Criqui MH, Langer RD, Fronek A, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. N Engl J Med 1992;326:381-6.

2. Criqui MH. Peripheral arterial disease--epidemiological aspects. Vasc Med 2001;6:3-7.

3. Aronow WS, Ahmed MI, Ekundayo OJ, Allman RM, Ahmed A. A propensity-matched study of the association of peripheral arterial disease with cardiovascular outcomes in community-dwelling older adults. Am J Cardiol 2009;103:130-5.

4. Criqui MH, Coughlin SS, Fronek A. Noninvasively diagnosed peripheral arterial disease as a predictor of mortality: results from a prospective study. Circulation 1985;72:768-73.

5. McDermott MM, Liu K, Criqui MH, et al. Ankle-brachial index and subclinical cardiac and carotid disease: the multi-ethnic study of atherosclerosis. Am J Epidemiol 2005;162:33-41.

6. Hirsch AT, Criqui MH, Treat-Jacobson D, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA 2001;286:1317-24.

7. Donnelly R. Assessment and management of intermittent claudication: importance of secondary prevention. Int J Clin Pract Suppl 2001;(119):2-9.

8. Novo S. Classification, epidemiology, risk factors, and natural history of peripheral arterial disease. Diabetes Obes Metab 2002;4 Suppl 2:S1-6.

9. Fowkes FG, Murray GD, Butcher I, et al. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. JAMA 2008;300:197-208.

10. Agnelli G, Cimminiello C, Meneghetti G, Urbinati S. Low ankle-brachial index predicts an adverse 1-year outcome after acute coronary and cerebrovascular events. J Thromb Haemost 2006;4:2599-606.

11. Vidula H, Tian L, Liu K, et al. Biomarkers of inflammation and thrombosis as predictors of near-term mortality in patients with peripheral arterial disease: a cohort study. Ann Intern Med 2008;148:85-93.

12. Khaleghi M, Kullo IJ. Aortic augmentation index is associated with the ankle-brachial index: a community-based study. Atherosclerosis 2007;195:248-53.

13. Brewer LC, Chai HS, Bailey KR, Kullo IJ. Measures of arterial stiffness and wave reflection are associated with walking distance in patients with peripheral arterial disease. Atherosclerosis 2007;191:384-90.

14. Kingwell BA, Waddell TK, Medley TL, Cameron JD, Dart AM. Large artery stiffness predicts ischemic threshold in patients with coronary artery disease. J Am Coll Cardiol 2002;40:773-9.

15. Papaioannou TG, Stamatelopoulos KS, Gialafos E, et al. Monitoring of arterial stiffness indices by applanation tonometry and pulse wave analysis: reproducibility at low blood pressures. J Clin Monit Comput 2004;18:137-44.

16. Wilkinson IB, Fuchs SA, Jansen IM, et al. Reproducibility of pulse wave velocity and augmentation index measured by pulse wave analysis. J Hypertens 1998;16:2079-84.

17. Zeymer U, Parhofer KG, Pittrow D, et al. Risk factor profile, management and prognosis of patients with peripheral arterial disease with or without coronary artery disease: results of the prospective German REACH registry cohort. Clin Res Cardiol 2009;98:249-56.

18. Redheuil A, Yu WC, Wu CO, et al. Reduced ascending aortic strain and distensibility: earliest manifestations of vascular aging in humans. Hypertension 2010;55:319-26.

19. Frimodt-Moller M, Nielsen AH, Kamper AL, Strandgaard S. Reproducibility of pulse-wave analysis and pulse-wave velocity determination in chronic kidney disease. Nephrol Dial Transplant 2008;23:594-600.

20. Chemla D, Nitenberg A, Teboul JL, et al. Subendocardial viability ratio estimated by arterial tonometry: a critical evaluation in elderly hypertensive patients with increased aortic stiffness. Clin Exp Pharmacol Physiol 2008;35:909-15.

21. Ikonomidis I, Tzortzis S, Papaioannou T, et al. Incremental value of arterial wave reflections in the determination of left ventricular diastolic dysfunction in untreated patients with essential hypertension. J Hum Hypertens 2008;22:687-98.

22. Saito M, Okayama H, Nishimura K, et al. Possible link between large artery stiffness and coronary flow velocity reserve. Heart 2008;94:e20.

23. Safar ME. Hemodynamic changes in elderly hypertensive patients. Am J Hypertens 1993;6:20S-3S.

24. O'Rourke MF, Safar ME. Relationship between aortic stiffening and microvascular disease in brain and kidney: cause and logic of therapy. Hypertension 2005;46:200-4.

25. Lieber A, Millasseau S, Bourhis L, et al. Aortic wave reflection in women and men. Am J Physiol Heart Circ Physiol 2010;299:H236-42.

26. Van Bortel LM, Struijker-Boudier HA, Safar ME. Pulse pressure, arterial stiffness, and drug treatment of hypertension. Hypertension 2001;38:914-21.

27. Weber T, Auer J, O'Rourke MF, et al. Arterial stiffness, wave reflections, and the risk of coronary artery disease. Circulation 2004;109:184-9.

28. Weber T, O'Rourke MF, Ammer M, Kvas E, Punzengruber C, Eber B. Arterial stiffness and arterial wave reflections are associated with systolic and diastolic function in patients with normal ejection fraction. Am J Hypertens 2008;21:1194-202.

29. London GM, Blacher J, Pannier B, Guerin AP, Marchais SJ, Safar ME. Arterial wave reflections and survival in end-stage renal failure. Hypertension 2001;38:434-8.

30. Buckberg GD, Fixler DE, Archie JP, Hoffman JI. Experimental subendocardial ischemia in dogs with normal coronary arteries. Circ Res 1972;30:67-81.

31. Buckberg GD, Kattus AA, Jr. Factors determining the distribution and adequacy of left ventricular myocardial blood flow. Adv Exp Med Biol 1973;39:95-113.

32. Amoh-Tonto CA, Malik AR, Kondragunta V, Ali Z, Kullo IJ. Brachial-ankle pulse wave velocity is associated with walking distance in patients referred for peripheral arterial disease evaluation. Atherosclerosis 2009;206:173-8.

LEGENDS

Table 1. Characteristics of the study population (n=65)

Age (years)	69 ± 11
Female, n (%)	17 (26)
Body height (cm)	170 ± 7.9
Weight (kg)	74.5 ± 12.6
Body mass index (kg/m^2)	25.7 ± 3.7
Cardiovascular risk factors, n (%)	
Hypertension	52 (80)
History of smoking	48 (74)
Diabetes	15 (23)
Dyslipidemia	39 (60)
Comorbidities, n (%)	
Coronary artery disease	19 (29)
Cerebrovascular disease	15 (23)
Renal insufficiency	8 (12)
Medication, n (%)	
Nitrates	2 (3)
ß-blockers	35 (54)
ACE inhibitors	28 (43)
Angiotensin receptor blockers	16 (25)
Calcium channel blockers	19 (29)
Diuretics	30 (46)
Lipid-lowering medication	54 (83)

Table entries are mean ± SD for quantitative variables and numbers (percentages) for categorical variables.

Table 2. Pressure characteristics of patients (n=65)

ABI	0.8 ± 0.2	(0.4 - 1.2)
AIx@75HR	31 ± 7	(17 - 47)
SEVR	141 ± 26	(90-230)
Heart rate (bpm)	67 ± 9	(48 - 89)
SBP (mmHg)	152 ± 21	(120 - 250)
DBP (mmHg)	81 ± 11	(60 - 110)
Brachial PP (mmHg)	71 ± 18	(40 - 150)
Central PP (mmHg)	59 ± 17	(29-135)

Table entries are mean ± SD (range). Bpm, beats per minute ; SBP, systolic blood pressure ; DBP, diastolic blood pressure ; PP, pulse pressure

Table 3. Variables associated with aortic augmentation index in patients with peripheral arterial disease

	Unrestricted Model				Restricted Model			
	Coef.	95% CI		p	Coef.	95% CI		p
ABI	-10.67	-18.36	-2.97	0.008	-11.5	-18.6	-4.5	0.002
Age, years	0.06	0.10	0.23	0.449				
Sex	0.17	-3.66	4.00	0.929				
Height, cm	-42.27	-63.38	-21.16	<0.001	-46.2	-62.93	-29.43	<0.001
Body mass index, kg/m^2	-0.45	-0.87	-0.024	0.039	-0.43	-0.80	-0.06	0.02
Smoker	5.20	1.54	8.86	0.006	3.6	0.60	6.59	0.02
Dyslipidaemia	0.25	-2.64	3.14	0.862				
Hypertension	0.56	-3.98	5.09	0.806				
Diabetes	0.10	-3.56	3.77	0.955				
Systolic blood pressure	0.02	-0.07	0.11	0.680				
Diastolic blood pressure	0.23	0.06	0.40	0.009	0.24	0.12	0.36	<0.001
Comorbidities	-0.99	-4.24	2.27	0.546				
Antihypertensive drugs	2.49	-1.39	6.36	0.203				

Table 4. Variables associated with subendocardial viability ratio in patients with peripheral arterial disease

	Unrestricted Model				Restricted Model			
	Coef.	95% CI		p	Coef.	95% CI		p
ABI	37.29	4.12	70.45	0.028	33.17	2.29	64.06	0.04
Age, years	0.02	-0.69	0.73	0.952				
Sex	-17.05	-33.55	-0.54	0.043	-14.96	-30.06	0.14	ns
Height, cm	96.55	5.59	187.52	0.038	76.76	-6.67	160.18	ns
Body mass index, kg/m^2	0.36	-1.47	2.18	0.696				
Smoker	1.35	-14.4	17.12	0.864				
Dyslipidaemia	-1.08	-13.54	11.39	0.863				
Hypertension	14.07	-5.48	33.61	0.155				
Diabetes	-8.07	-23.85	7.72	0.310				
Systolic blood pressure	-0.72	-1.12	-0.32	0.001	-0.61	-0.96	-0.25	0.001
Diastolic blood pressure	0.99	0.26	1.71	0.009	0.80	0.17	1.43	0.01
Comorbidities	7.44	-6.58	21.46	0.292				
Antihypertensive drugs	0.24	-16.46	16.93	0.978				

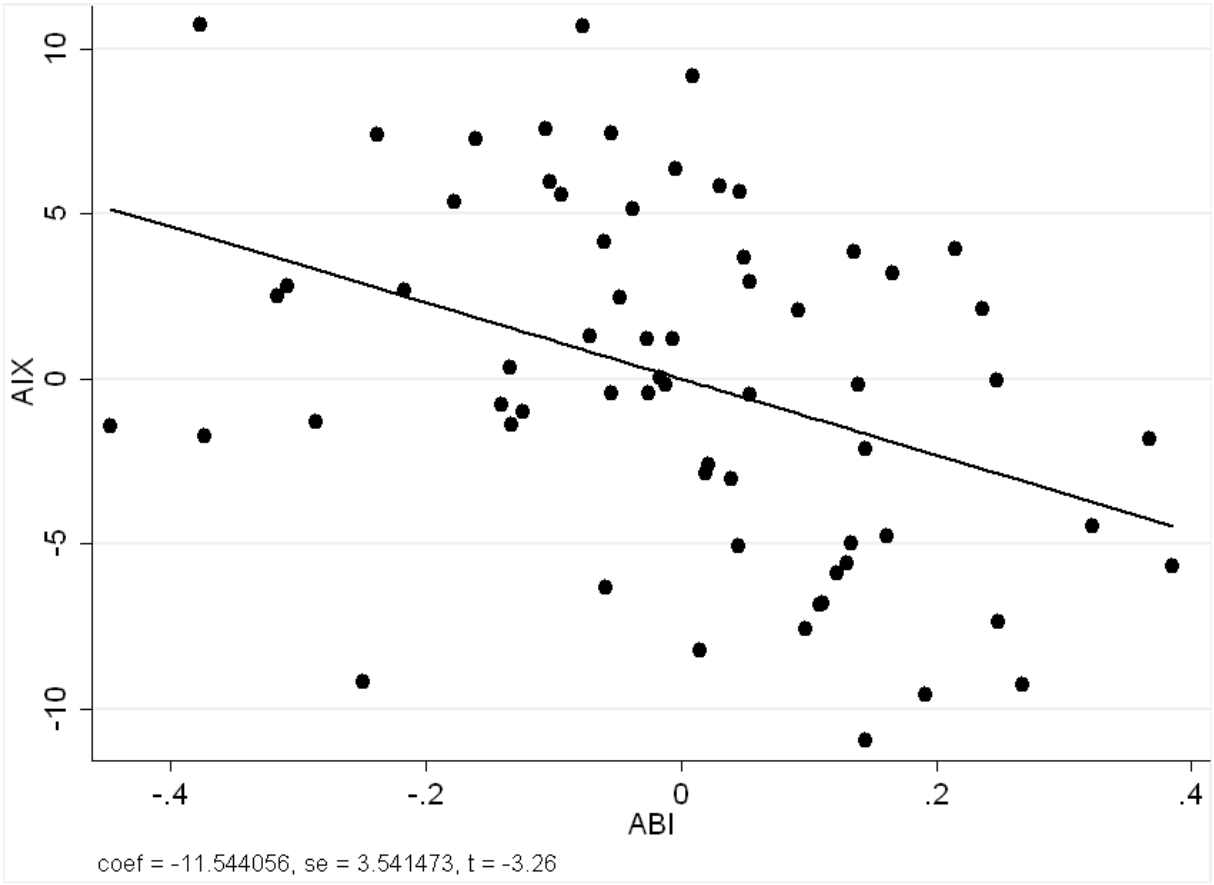

Figure 1. Partial regression plot for aortic augmentation index and ankle-brachial pressure index in patients with peripheral arterial disease

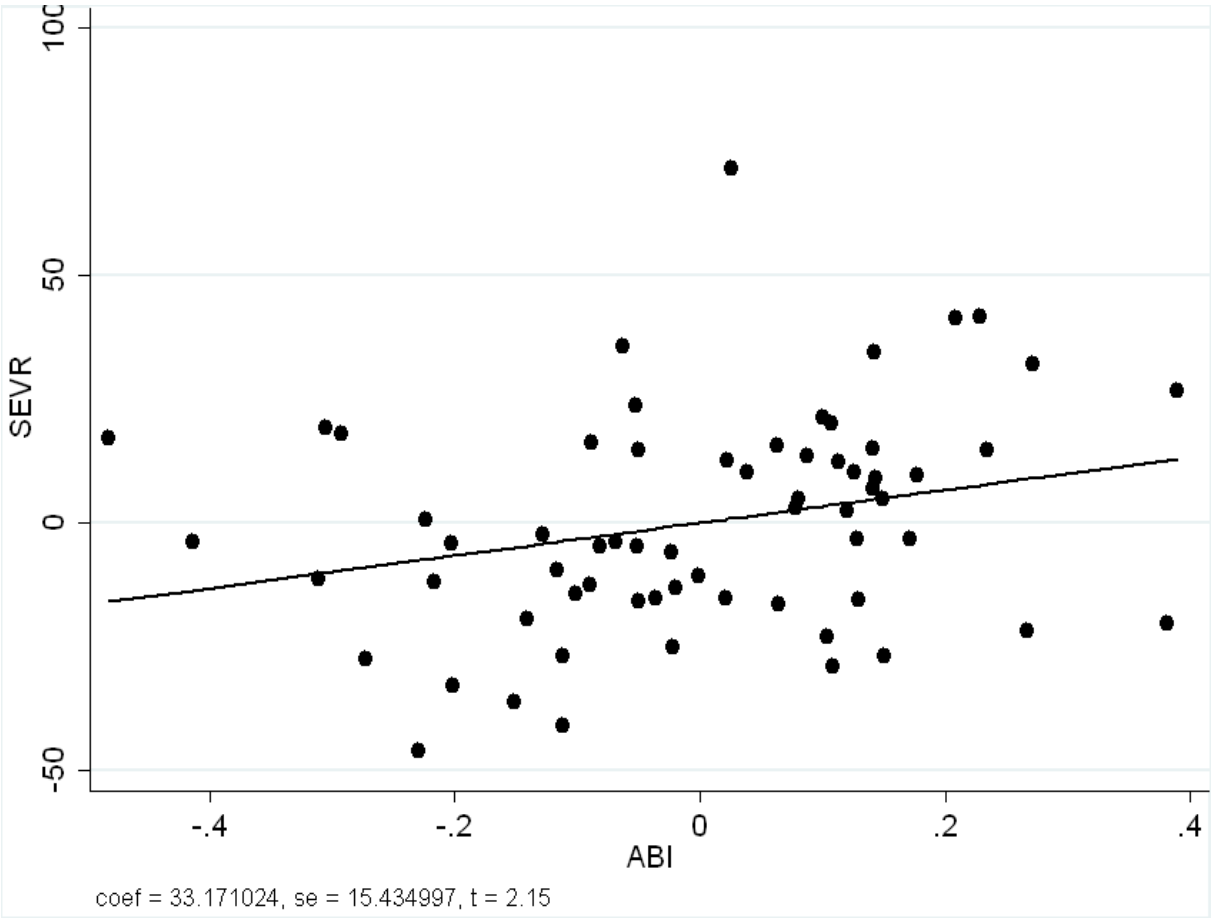

Figure 2. Partial regression plot for subendocardial viability ratio and ankle-brachial pressure index in patients with peripheral arterial disease

VERDANKUNGEN

Ich möchte allen, die mir die Arbeit an meiner Dissertation ermöglichten und erleichterten ganz herzlich danken:

Frau Prof. Amann-Vesti, die mir diese Dissertation überhaupt ermöglichte.

PD Dr. Marc Husmann für die engagierte Betreuung und die angenehme Zusammenarbeit.

Peter Fennema für die Unterstützung bei der statistischen Auswertung und die anregenden Diskussionen.

Meinen Eltern, für die langjährige emotionale und finanzielle Unterstützung während meiner gesamten Ausbildungszeit.

CURRICULUM VITAE

Kathrin Mosimann Fennema von Lauperswil, Bern

24.07.1972	Geboren in Zürich
1979 – 1988	Primarschule und Sekundarschule in Zürich und Thalwil
1988 – 1992	Gymnasium Maturitätstyp D mit kleinem Latinum an der Kantonsschule Enge Zürich
1993 – 1995	Studium Phil I in Anglistik, Geschichte, Kunstgeschichte an der Universität Zürich
1995 – 1998	Ausbildung an der Schule für klassische Naturheilkunde Zürich
1995 – 2000	Teilzeitarbeit im Institut für medizinische und molekulare Diagnostik (IMD AG) in Labor und Administration in Zürich
2000 – 2007	Studium der Humanmedizin an der Universität Zürich
2007	Eidg. Examen Humanmedizin 10/2007
2008	Assistenzärztin Abteilung Neurorehabilitation, Reha Rheinfelden, Rheinfelden, AG
2009 - 2011	Assistenzärztin Abteilung Medizin, Spital Uster, Uster, ZH
Seit 08/2011	Assistenzärztin Abteilung Medizin, Stadtspital Triemli, ZH