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Original Study

Aging and Outcome in Patients With Peripheral Artery Disease and Critical Limb Ischemia

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A B S T R A C T

Background, objectives, design: Aging of the population is one of the major challenges facing public health systems. The impact of aging on acute and long-term outcome of patients with peripheral artery disease (PAD) and critical limb ischemia (CLI) is currently not sufficiently clarified. This analysis consists of comprehensive, anonymized data obtained from the largest public health insurance in Germany.
Results: A total of 41,740 PAD patients with an index hospitalization between January 1, 2009, and December 31, 2011, and a follow-up time up to 4 years were included (40-49 years: n = 1179; 50-59 years: n = 5415; 60-69 years: n = 10,565; 70-79 years: n = 13,313; 80-89 years: n = 9714; and 90-100 years: n = 1554). Advanced age was associated with female gender (men-women ratio up to 1:3.3), less smoking, less frequent obesity, more often chronic heart failure (up to 9-fold), chronic kidney disease (up to 4-fold), fewer angiographies (up to 0.8-fold), fewer endovascular (up to 0.5-fold) and surgical revascularizations (up to 0.9-fold), higher rates of amputation (up to 2.5-fold), acute renal failure (up to 3.7-fold), in-hospital mortality (up to 12-fold), myocardial infarction (up to 2.8-fold), ischemic stroke (up to 1.5-fold), infection (up to 1.4-fold), and sepsis (up to 1.8-fold) (each $P < .001$). During follow-up, advanced age was a highly significant independent predictor of long-term mortality, myocardial infarction, and stroke (each $P < .001$). Lengths of hospital stay (up to 1.3-fold longer) and reimbursement costs (up to 1.1-fold higher) were clearly associated with advanced age (each $P < .001$).
Conclusions: This study demonstrates the impact of aging on morbidity, in-hospital treatment, complications, and acute and long-term outcome of PAD patients.

Peripheral artery disease (PAD) is worldwide one of the most common diseases, currently affecting more than 200 million people worldwide[1] with increasing economic impacts on health systems regarding treatment and costs.[2] PAD is associated with markedly higher rates of cardiovascular events and mortality[3] compared with the general population. This applies especially to critical limb ischemia (CLI), which comprises advanced PAD stages. The prevalence of PAD seems to increase markedly with rising age.[1,2,4–7]

Advanced age is discussed as one of the strongest risk factors for morbidity,[8,9] higher rates of myocardial and cerebrovascular events,[10] amputation,[2] and mortality in PAD patients.[8–10] However, it is currently not sufficiently clear to which extent severity, morbidity, and outcome vary in the different decades of life of PAD patients. Comprehensive data about the impact of aging on morbidity and the acute and long-term outcomes in PAD patients are currently still missing. Therefore, the aim of this study was to evaluate the age-related morbidity, in-hospital mortality, treatment, amputation and complication rates, and long-term outcome of PAD and CLI patients in this large-scale cohort.

Materials and Methods

Data Source, Study Population, and Inclusion Criteria

The analysis consists of comprehensive data obtained from the largest public health insurance in Germany (Barmer GEK), which insures more than 8 million people (currently representing 10% of the entire German population). We received anonymized data of all

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patients who had an index hospitalization between January 1, 2009, and December 31, 2011, with a main or secondary diagnosis of lower limb PAD as described elsewhere in detail.[10] Patients were categorized into six age categories, in accordance with other studies[11,12]: 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years, 80 to 89 years, and 90 to 100 years.

Diagnoses, Operations Procedure Codes, and Costs

All diagnoses were coded in accordance with the German Modification of the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). Additionally, all diagnostic, endovascular, and surgical procedure codes on the basis of the German procedure classification [Operationen und Prozedurenschlüssel (OPS)] were obtained. Code I70.20 or I70.21 labeled PAD Rutherford stages 1 to 3; code I70.22, Rutherford stage 4; code I70.23, Rutherford stage 5; and code I70.24, Rutherford stage 6.

Moreover, all in-hospital costs including in-hospital measures, for example, drugs, catheters, and blood products, were included in this analysis. Any kinds of costs resulting from outpatient care were not included in the analysis.

Follow-up Data

The follow-up period started with the date of discharge of the index hospitalization. All in- and outpatient cardiovascular diagnoses and procedure codes were obtained over a minimum period of 24 months after discharge until December 31, 2012. Primary clinical endpoints are death, amputation, myocardial infarction, and ischemic stroke.

Statistics

Categorical variables are presented as absolute numbers and percentages of the total numbers. Continuous variables were illustrated as mean ± standard deviation and compared using analysis of variance *F* tests. Dichotomous parameters were compared via chi-square test. Event rates during follow-up were illustrated via Kaplan-Meier models. Analyses of the prognostic value of baseline parameters regarding long-term outcomes were made by multivariable Cox regression models. Results are presented as hazard ratios (HRs) and 95% confidence intervals (CIs). All tests were performed 2-sided. *P* values $< .05$ were considered statistically significant.

Ethics Considerations

The study is based entirely on anonymized data from a large German health insurance and therefore does not require approval from ethics committees according to local legal requirements.

Results

A total of 41,740 patients fulfilled the inclusion criteria mentioned above. Advanced age was associated with female gender (men-women ratio from 1:0.5 up to 1:3.3), less smoking, less common obesity, and more cases of chronic heart failure (up to 9-fold) and chronic kidney disease (up to 4-fold). The proportions of patients with classical cardiovascular risk factors (hypertension, dyslipidemia, diabetes) were associated up to the seventh life-decade with increasing age (each $P < .001$).

Proportions with Rutherford stages 5 and 6 increased markedly with increasing age ($P < .001$). Vice versa, those with Rutherford stages 1 to 3 decreased ($P < .001$) with higher age. Baseline characteristics and comorbidities of all patients with regard to the age categories are presented in Table 1.

In-hospital Treatment and Complications

The frequency of arterial angiographies increased up to the eighth life-decade ($P < .001$), but advanced age (>80 years) was associated with fewer angiographies (up to 0.8-fold). Those of endovascular and surgical revascularizations decreased with increasing age (up to 0.5-fold and 0.9-fold, respectively, each $P < .001$). Vice versa, increasing age was associated with distinctly higher amputation rates (up to 2.5-fold).

Advanced age was associated with markedly higher in-hospital complication rates: acute renal failure (up to 3.7-fold), in-hospital mortality (up to 12-fold), myocardial infarction (up to 2.8-fold), ischemic stroke (up to 1.5-fold), infection (up to 1.4-fold), and sepsis (up to 1.8-fold). Details of in-hospital treatment and outcome during the index hospitalization are presented in Table 2.

Vascular Procedures in Amputated Patients

During their index hospitalization, a total of 4276 CLI patients (Rutherford stages 4 to 6) were amputated. With advanced age, marked differences appeared within the various age categories: amputated patients who underwent only an angiography represented

Table 1
Baseline Characteristics and Comorbidities With Regard to the Impact of Age

	40-49 y	50-59 y	60-69 y	70-79 y	80-89 y	90-100 y	Total	*P*
Patients, n (% of all)	1179 (2.8)	5415 (13.0)	10565 (25.3)	13313 (31.9)	9714 (23.3)	1554 (3.7)	41740 (100.0)	
Rutherford categories, n (%)								**<0.001**
RF 1-3	744 (63.1)	3580 (66.1)	6525 (61.8)	6973 (52.4)	3088 (31.8)	240 (15.4)	21150 (50.7)	
RF 4	154 (13.1)	657 (12.1)	1230 (11.6)	1642 (12.3)	1419 (14.6)	225 (14.5)	5327 (12.8)	
RF 5	112 (9.5)	469 (8.7)	1249 (11.8)	2163 (16.2)	2446 (25.2)	452 (29.1)	6891 (16.5)	
RF 6	169 (14.3)	709 (13.1)	1561 (14.8)	2535 (19.0)	2761 (28.4)	637 (41.0)	8372 (20.1)	
Women, n (%)	417 (35.4)	1623 (30.0)	3647 (34.5)	5609 (42.1)	6025 (62.0)	1202 (77.3)	18523 (44.4)	**<0.001**
Hypertension, n (%)	549 (46.6)	3193 (59.0)	7156 (67.7)	9690 (72.8)	6835 (70.4)	1028 (66.2)	28451 (68.2)	**<0.001**
Obesity, n (%)	101 (8.6)	551 (10.2)	994 (9.4)	1040 (7.8)	352 (3.6)	18 (1.2)	3056 (7.3)	**<0.001**
Dyslipidemia, n (%)	351 (29.8)	1817 (33.6)	3671 (34.7)	4559 (34.2)	2349 (24.2)	181 (11.6)	12928 (31.0)	**<0.001**
Smoking, n (%)	356 (30.2)	1389 (25.7)	1787 (16.9)	912 (6.9)	230 (2.4)	4 (0.3)	4678 (11.2)	**<0.001**
Diabetes, n (%)	277 (23.5)	1412 (26.1)	3369 (31.9)	4859 (36.5)	3185 (32.8)	420 (27.0)	13522 (32.4)	**<0.001**
CAD, n (%)	144 (12.2)	916 (16.9)	2521 (23.9)	3887 (29.2)	2632 (27.1)	356 (22.9)	10456 (25.1)	**<0.001**
Chronic heart failure, n (%)	26 (2.2)	205 (3.8)	685 (6.5)	1341 (10.1)	1559 (16.0)	304 (19.6)	4120 (9.9)	**<0.001**
CKD, n (%)	100 (8.5)	514 (9.5)	1575 (14.9)	3213 (24.1)	3187 (32.8)	549 (35.3)	9138 (21.9)	**<0.001**
Malignancies, n (%)	6 (0.5)	50 (0.9)	175 (1.7)	314 (2.4)	206 (2.1)	23 (1.5)	774 (1.9)	**<0.001**

Note: bold values are statistically significant $P < .05$.
CAD, coronary artery disease; CKD, chronic kidney disease; RF, Rutherford category; SD, standard deviation.
Data of patients with an index hospitalization of peripheral artery disease (main or secondary diagnosis) between January 1, 2009, and December 31, 2011, obtained from a large German health insurance.