Journal Pre-proof

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PII: S1078-5884(23)00060-6

DOI: https://doi.org/10.1016/j.ejvs.2023.01.026

Reference: YEJVS 8648

To appear in: *European Journal of Vascular & Endovascular Surgery*

Received Date: 1 July 2022

Revised Date: 18 November 2022

Accepted Date: 13 January 2023

Please cite this article as: Roedl K, Daniels R, Theile P, Kluge S, Müller J, Behrendt C-A, The Independent Impact of Peripheral Arterial Disease on Mortality in Nonagenarians and Centenarians Who Were Treated in an Intensive Care Unit: A Consecutive Cohort of 1 108 Patients, *European Journal of Vascular & Endovascular Surgery*, https://doi.org/10.1016/j.ejvs.2023.01.026.

The Independent Impact of Peripheral Arterial Disease on Mortality in Nonagenarians and Centenarians Who Were Treated in an Intensive Care Unit: A Consecutive Cohort of 1 108 Patients

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WHAT THIS PAPER ADDS

In this large up to date consecutive cohort of 1 108 critically ill nonagenarians and centenarians treated in an intensive care unit between 1 January 2008 and 30 April 2019, a total of 24% were diagnosed with any peripheral arterial disease (PAD). For the first time, the independent impact of PAD on short term and long term mortality was determined while PAD outweighed the effect of higher age in this study population. Forty one per cent of the patients with PAD died during the hospital stay (*vs.* 26% in a comparison group, hazard ratio 1.97, $p < .001$).

Objective: To investigate the clinical characteristics, risk factors, and outcomes of inpatients with peripheral arterial disease (PAD) including lower extremity PAD, abdominal aortic aneurysm (AAA), and carotid artery disease in a large cohort of critically ill patients aged ≥ 90 years.

Methods: A retrospective analysis was conducted of all adult patients aged ≥ 90 years consecutively admitted to the intensive care unit at a tertiary care centre in Hamburg, Germany, between 1 January 2008 and 30 April 2019. Multivariable regression and Kaplan–Meier methods were used to determine the independent impact of PAD on short term and long term mortality endpoints. The analyses were adjusted for confounding by several sociodemographic and clinical parameters including Charlson Comorbidity Index (CCI) and established clinical risk scores.

Results: A total of 1 108 eligible patients were identified (92.3 years, 33% men). Of these, 24% had PAD (9% lower extremity PAD, 2% AAA, 15% coronary artery disease) and 76% did not have any history of PAD and were used as a comparison group. When compared with the comparison group, patients with PAD had a higher CCI (2 *vs.* 1, $p < .001$), more often chronic kidney disease (28% *vs.* 21%, $p = .019$), and renal replacement therapy (5% *vs.* 2%, $p = .016$). Furthermore, they needed vasopressors (48% *vs.* 40%, $p = .027$) and parenteral nutrition (10% *vs.* 6%, $p = .041$) more often. After adjusting for confounding, PAD was independently associated with increased in hospital (hazard ratio [HR] 1.97, 95% confidence interval [CI] 1.39 – 2.81, $p < .001$) and long term mortality (HR 1.32, 95% CI 1.05 – 1.66, $p = .019$).

Conclusion: One out of four critically ill nonagenarians and centenarians in an ICU in Germany had PAD. PAD was associated with both higher short and long term mortality while its impact outweighed higher age. Future studies should address this increasingly important population beyond 89 years of age.

Keywords: Critical illness, Critically ill, Intensive care unit, Nonagenarians, Peripheral vascular disease, Vascular disease, Very elderly

<H1>INTRODUCTION

Due to improvements in preventive medicine, medical innovations, and best medical treatment, the life expectancy of global populations has increased rapidly. The population of very old patients is expected to grow further; there will be over 30 million people who are 90 years or older (nonagenarian, centenarian) by 2030.[1] To date, about 15% of critically ill patients in the intensive care unit (ICU) are aged ≥ 80 years and 1% are aged ≥ 90 years.[2,3]

Peripheral arterial disease (PAD) including lower extremity PAD, carotid artery disease, and abdominal aortic aneurysm (AAA), is a common manifestation of systemic atherosclerosis.[4–8] In 2015, almost 237 million patients were affected by PAD worldwide with an increasing prevalence of approximately 15–20% in patients aged between 70 and 74 years, and further increasing prevalence with age.[4,9] Especially in octogenarians and nonagenarians there are data suggesting an increasing prevalence of PAD with more than 20% having PAD in at least one arterial territory.[10] According to the World Health Organization (WHO) and national death statistics, PAD is among the three most common causes of death, which emphasizes the burden of this common disease. Despite this, the impact of PAD on outcomes in patients aged over 90 years remains understudied, especially when focusing on inpatients requiring advanced treatment in an ICU.

This study aimed to investigate the clinical characteristics, risk factors, and outcomes of inpatients with PAD in a large cohort of critically ill patients aged ≥ 90 years in a tertiary care university hospital.

<H1>METHODS

<H2>Study design, setting, and ethics

Data of all adult nonagenarians (90 – 99 years) and centenarians (≥ 100 years) consecutively admitted to the Department of Intensive Care Medicine at the University Medical Centre Hamburg-Eppendorf (Hamburg, Germany) between 1 January 2008 and 30 April 2019, were retrospectively analysed. The department covers 12 intensive care wards and provides health benefits for all critically ill adult (≥ 18 years) patients of the university hospital with a total capacity of 140 beds. The Ethics Committee of the Hamburg Chamber of Physicians was informed about the study (No.: 2022-300219-WF). Due to the retrospective nature of the study and the de-identified study data, the need for explicit informed consent was waived. Information regarding mortality up to one year was obtained from the national death register of Germany at least one year after admission to ICU.

<H2>Inclusion and exclusion criteria

All consecutively treated inpatients aged ≥ 90 years who were admitted to the ICU were included in the study. Patients < 90 years of age and patients with incomplete clinical data (*n* = 17, 1.5%) were excluded (Fig. 1).

<H2>Data collection

Data was collected through a digital patient data management system (PDMS, Integrated Care Manager (ICM), Version 9.1 – Draeger Medical, Lubeck, Germany). The extracted data included age in years, dichotomised sex, comorbidities according to the Charlson Comorbidity Index (CCI), primary admission diagnosis (medical, surgical – elective, surgical – emergency; the term surgical refers to all surgical procedures), total length of ICU and hospital stay in days, survival during ICU and hospital stay, treatment modalities and organ support (mechanical ventilation, vasopressor, renal replacement therapy, blood transfusions, applied antibiotics, applied antivirals), and routine laboratory parameters. Routine laboratory assessment was performed on a daily basis within clinical routine.

<H2>Study definitions and patient management

All data were derived retrospectively. The variable PAD included the entities 1) PAD of the lower extremities usually diagnosed by an ankle brachial index (ABI) ≤ 0.9 or any reported history of intermittent claudication or chronic limb threatening ischaemia;[11] 2) usually diagnosed by an infrarenal aortic diameter ≥ 3.0 cm or any reported history of an AAA;[12] 3) carotid artery disease usually defined by any diagnosis of an intimal media thickness of ≥ 1.0 mm or reported history of carotid artery plaques.[13,14]

Severity of illness was evaluated by Sequential Organ Failure Assessment (SOFA)[15] and Simplified Acute Physiology (SAPS II)[16] score on admission. The CCI[17] was calculated in all patients. Sepsis and septic shock were defined according to the 2016 Third International Consensus Definition for Sepsis and Septic Shock.[18]

<H2>Statistical analysis

Data are presented as absolute numbers and relative frequency or median and interquartile range (IQR). Categorical variables were compared via chi-square analysis or Fisher's exact test, as appropriate. Continuous variables were compared via Mann–Whitney U test or Student *t* test, as appropriate. Factors associated with PAD and mortality were clinically assessed. A multivariable logistic regression with PAD as the dependent variable and clinical variables as covariables was used. A multivariable Cox proportional hazards model was used to estimate the effect of PAD on in hospital and midterm survival.

In both models, a stepwise backward elimination approach was used that gradually reduces the initial model; variables that caused a change in estimates > 10% remained in the model. Survival function estimates were calculated using the Kaplan–Meier method and were compared by the log rank test. Further, a landmark analysis was performed for long term outcomes excluding all patients dying in hospital. Patients alive at the landmark point were categorised PAD and non-PAD. A sensitivity analysis was run with the hospital surviving patients included in the PAD along with the patients who had non-PAD. Statistical analysis was conducted using IBM SPSS Statistics Version 24.0 (IBM Corp., Armonk, NY, USA). A p value $< .050$ was considered statistically significant. No correction was applied for multiple hypothesis testing. A complete case exclusion was applied for missing variables. The study was prepared in accordance with the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) recommendations.[19]

<H1>RESULTS

<H2>Baseline characteristics of the study population

During the study period from 1 January 2008 to 30 April 2019, a total number of 92 958 patients were treated at the study centre ICU. Overall, 1.2% (1 108/92 958) were aged > 89 years and were included in the study (Fig. 1). From the total cohort, 24% of patients (*n* = 264) were identified with PAD and 76% (*n* = 844) without PAD. In terms of vascular diseases, coronary artery disease was observed in 15% of patients (*n* = 171), lower extremity PAD in 9% (*n* = 101), and AAA in 2% (*n* = 24).

<H2>Comparison of clinical characteristics in patients with versus without peripheral arterial disease (crude comparison)

The baseline characteristics of patients with *versus* without PAD are shown in Table 1. Demographic characteristics including age, sex, and BMI were comparable in both strata. Primary admission cause to the ICU was medical (34% for PAD *vs.* 34%, *p* = .95), elective surgery (29% for PAD *vs.* 39%, *p* = .003), and emergency surgery (36% for PAD *vs.* 26%, *p* = .003). The CCI was 2 (IQR 1, 3) in median compared with 1 (IQR 0, 2) points in patients with and without PAD (*p* < .001), respectively. Detailed characteristics on comorbidities are shown in Supplementary Table S1. Patients with PAD had comparable disease severity on admission, represented by SAPS II (38 *vs.* 36 points, *p* = .22), SOFA (3 *vs.* 2 points, *p* = .13) on admission and after 24 hours (2 *vs.* 2 points, *p* = .069). Patients with PAD were mechanically ventilated in 37% (*n* = 97) compared with 35% (*n* = 292) in those without PAD (*p* = .52). Thereby, the duration of MV was 0.7 (IQR 0.27, 1.38) and 0.5 (IQR 0.18, 1.17) days in patients with and without PAD, respectively (*p* = .11). Vasopressor therapy (48% *vs.* 40%, *p* = .027), renal replacement therapy (5% *vs.* 2%, *p* = .016), and parenteral nutrition (10% *vs.* 6%, *p* = .041) was more frequent in patients with PAD. Tracheostomy (2% *vs.* 1%, *p* = .66) was observed similarly in both groups. The requirement of transfusion of red blood cells, thrombocytes, or fresh frozen plasma was comparable in both groups. Further, detailed laboratory and blood gas analysis characteristics are shown in Table 1.

<H2>Outcomes of patients with versus without peripheral arterial disease (crude comparison)

The median stay of the entire cohort in the ICU and hospital was 1.6 (IQR 0.9, 3.5) and 11 (IQR 7, 16.6) days, respectively. Overall, 18% (*n* = 201) died in the ICU and 30% (*n* = 331) during the hospital stay. During the ICU stay, 23% (*n* = 62) of the patients with PAD died (*vs.* 16%, *n* = 139, without PAD, *p* = .010). During the total in hospital stay, 41% (*n* = 108) of the patients with PAD died (*vs.* 26%, *n* = 223, *p* < .001). The median length of stay at the ICU and in the hospital was 1.7 (IQR 0.9, 4.1) and 11.1 (IQR 5.9, 17.2) days in patients with PAD and 1.5 (IQR 0.9, 3.2) and 11.0 (IQR 7.0, 16.5) in patients without PAD, respectively.

The Kaplan–Meier survival estimates including long term follow up are depicted in Fig. 2. The sensitivity analysis regarding the effect of PAD on mortality (Landmark analysis) was confirmative (Supplementary Fig. S1).

Patients who survived the hospital stay (n = 777) were discharged to their home in 28% (n = 28) with PAD and without PAD 25% (n = 153) (p = .077), nursing facility in 27% (n = 42) and 15% (n = 91) (p < .001), rehabilitation facility in 41% (n = 64) and 45% (n = 282) (p = .33), and another hospital in 13% (n = 21) and 15% (n = 95) (p = .57). The discharge destination was unknown for one patient.

<H2>Logistic and Cox regression analysis for factors associated with in hospital and 30 day mortality

Multivariate regression analysis identified PAD (odds ratio [OR] 1.973, 95% confidence interval [CI] 1.387 – 2.808; p < .001) as an independent factor associated with short term mortality during the hospital stay. The Cox regression analysis identified PAD (hazard ratio [HR] 1.316, 95% CI 1.046 – 1.656; p = .019) as an independent factor associated with long term mortality (Tables 2 and 3).

<H1>DISCUSSION

In this large consecutive cohort of critically ill nonagenarians and centenarians who were treated at a tertiary care ICU in Germany, one out of four patients suffered from PAD. When compared with the comparison group, these patients underwent emergency surgery more often, had a higher comorbidity index, were more often dialysis dependent, and died more often during both the ICU and hospital stay. After adjusting for confounding, the atherosclerotic disease burden contributed substantially to worse outcomes when compared with very old patients without co-existing PAD. Moreover, the impact of peripheral atherosclerosis outweighed higher age in this study population.

According to data from the Organisation for Economic Co-Operation and Development (OECD), the population-based life expectancy at birth increased by approximately 11 years from 69.7 in 1970 to 81.0 in 2019. As of today, ICU patients aged ≥ 90 years represent a rapidly growing population while approximately 64% of these patients are in need of long term care.[20]

Cardiovascular diseases comprise a heterogeneous group of chronic progressive conditions that are the leading cause of death globally. Patients with PAD and especially those with multisite artery disease face devastating outcomes during the hospital stay and beyond.[6]

In recent registry cohorts, the five year amputation and death rates reached 13 – 50% in patients with intermittent claudication and 50 – 90% in patients with chronic limb threatening ischaemia.[21–23] Thereby, data derived from the Global Burden of Disease study emphasised that the age specific PAD death rate increased markedly with age, particularly in patients aged ≥ 80 years also over time.[24]

Against this background it appears interesting that recent practice guidelines on vascular disease did not comprehensively cover the management of this increasingly relevant population.[6,25] A possible explanation for this is that only very few studies specifically addressed populations aged > 89 years.

In a two centre retrospective observational study of acute ischaemic stroke patients who underwent mechanical thrombectomy, only 7% were aged 90 – 99 years but the outcomes were comparable with those of octogenarians. The authors concluded that it did not appear justifiable to withhold invasive therapy, although the absolute treatment effect among nonagenarians remained unknown.[26] In another retrospective review of 32 421 patients who underwent open heart surgery, only 0.4% were nonagenarians. When compared with octogenarians, the nonagenarians exhibited similar mortality and complication rates during the hospital stay.[27] This finding, however, was contrasted by results from interventional aortic valve therapy in which 19% of patients were aged 90 – 99 years. While major vascular complications and in hospital mortality rate were higher in nonagenarians, the overall technical success was high and comparable with that of younger cohorts.[28] Siam *et al*. used a large database from an academic centre to determine factors associated with outcomes of surgery in patients aged ≥ 90 years. Between 2014 and 2018, 198 nonagenarians were included (38% elective). Emphasised by considerably low mortality rates after elective surgery, the authors concluded that surgery can be safely performed with acceptable two year outcomes, but emergency surgery for oncology carried rather dismal outcomes.[29]

In terms of PAD, the existing evidence base remains limited to very few observational cohorts. Casajuana Urgell *et al*. used a single centre institutional database covering 171 nonagenarians with chronic limb threatening ischaemia who were treated between 2005 and 2019. Almost one third of the patients had a direct indication for amputation or palliative care at presentation. Besides higher age (> 92 years), a low haemoglobin level, congestive heart failure, non-severe dementia, and limited mobility (wheelchair) were associated with worse survival.[30] Kumar *et al*. used data derived from the National Surgical Quality Improvement Program (NSQIP) dataset in the United States to determine outcomes in patients aged ≥ 90 years who had undergone abdominal aortic aneurysm repair from 2005 to 2017. Among 1 356 patients, 91% had undergone endovascular repair and 9% open surgery. The overall 30 day mortality was only 10.4% while nonagenarians had an incrementally increased, but acceptable, risk with EVAR in elective and emergent cases compared with that reported for octogenarians and cohorts not selected for age. Dependent status, higher American Society of Anaesthesiologists (ASA) classification, emergent repair, and open surgery were associated with mortality.[31]

The current study results may help to extend the limited knowledge by including a very old and critically ill population to determine the complex interaction between age and PAD. In line with previous cohorts, nonagenarians and centenarians had markedly high mortality rates during the ICU and hospital stay that were comparable with those of patients who were treated at ICU units after out of hospital cardiac arrest.[32,33]

Interestingly, while the overall risk profile and certain parameters were broadly similar between both comparison groups, the diagnosis of PAD was clearly associated with higher short and long term mortality in multivariable regression models. Especially during the hospital stay, the impact of PAD outweighed higher age and established comorbidity indices while landmark analyses emphasised that the association between PAD and long term mortality rates was less robust. It appears important to note that 15% of the patients had coronary artery disease. Systemic atherosclerosis affects different vascular beds and affects end organ microcirculation and perfusion in a multifactorial manner.

Besides its strengths, the current study has also limitations. Firstly, the non-randomised study design led to the possibility that residual confounding may have affected the relationship between the index diseases and outcomes of interest. This remains an unsolved challenge of observational research in general, but robust methods were applied and comorbidity indices established to reduce the inherent risk. Furthermore, the inclusion of a hospitalised cohort introduces a possible selection bias. The generalisability of the current study findings to non-hospitalised elderly remains unknown until further studies test the generated hypotheses on outpatient populations. Unfortunately, it is commonly known that prospective epidemiological cohorts and screening studies seldomly enrol participants aged > 80 years. Secondly, although the current study could only include data from a single centre, the intensive care department comprised a total of 140 beds and all medical specialties at a tertiary care centre in a large metropolitan area. Thirdly, the detection of the index diseases depended on various factors, and it could not be ruled out that undiagnosed PAD impaired the models. However, it appears rather unlikely that inpatients aged > 89 years have never been diagnosed for these chronic conditions in either systematic or opportunistic screening examinations. Lastly, although of increasing interest, the current study could not cover the complex relationship between patient frailty and poor outcomes.

Considering the current study findings, it appears reasonable to propose increased awareness among intensive care physicians and nurses to underline the potential impact of PAD and multisite artery disease on morbidity and mortality. Likewise, future studies are needed to expand the limited knowledge about this increasingly important population of very old patients with critical illness. While both intensive care and health services research entered the digital era long ago, it appears possible to use the rapidly growing information and sophisticated big data analytics to identify those who are in need of exceedingly intensive care. This explorative study may generate the first hypotheses to launch further projects.

<H2>Conclusion

In this large consecutive single centre database on 1 108 critically ill nonagenarians and centenarians on an ICU in Germany, one out of four patients had PAD. The diagnosis of any PAD was associated with both higher short and long term mortality while its impact outweighed higher age. Future studies should address this increasingly important population aged > 89 years.

CONFLICT OF INTEREST

P.T., R.D., J.M. and C.-A.B. do not report any conflicts of interest. S.K. received research support from Ambu, E.T.View Ltd, Fisher & Paykel, Pfizer, and Xenios, lecture honoraria from ArjoHuntleigh, Astellas, Astra, Basilea, Bard, Baxter, Biotest, CSL Behring, CytoSorbents, Fresenius, Gilead, MSD, Orion, Pfizer, Philips, Sedana, Sorin, Xenios, and Zoll, and consultant honorarium from AMOMED, Astellas, Baxter, Bayer, Fresenius, Gilead, MSD, Pfizer and Xenios. K.R. received travel support from Gilead, and reports no other potential conflict of interest relevant to this article.

FUNDING

This study was supported exclusively by institutional funds of the Department of Intensive Care Medicine.

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Figure 1. Flowchart of the study to investigate the clinical characteristics, risk factors, and outcomes of 1 108 critically ill nonagenarians, 264 with and 844 without peripheral arterial disease (PAD), at a tertiary care centre in Hamburg, Germany, between 1 January 2008 and 30 April 2019. ICU = intensive care unit.

Figure 2. Kaplan–Meier survival estimates stratified according to the presence of peripheral arterial disease (PAD); follow up information was missing for 18 patients (1.6%).

Table 1. Characteristics of 1 108 patients, 264 with and 844 without peripheral arterial disease (PAD), intensive care unit (ICU) at a tertiary care centre in Hamburg, Germany, between 1 January 2008 an

Variables	**All (*n* = 1 108)**	**PAD (*n* = 264)**	**Non-PAD (*n* = 844)**
Age – y	92.3 (91.0, 94.2)	92.4 (91.2, 94.4)	92.2 (90.9, 94.1)
Men	361 (33)	87 (33)	274 (31)
Median BMI – kg/m²	23.4 (21.0, 25.9)	23.9 (21.3, 26.2)	23.4 (20.9, 25.9)
Primary admission			
Medical	376 (34)	90 (34)	286 (34)
Elective surgery	409 (37)	77 (29)	332 (39)
Emergency surgery	316 (29)	94 (36)	222 (26)
Disease severity			
SAPS II, admission	36 (28, 47)	38 (28, 47)	36 (28, 47)
SOFA, admission	2 (1, 5)	3 (1, 6)	2 (1, 5)
SOFA, 24 h	2 (1, 4)	2 (1, 5)	2 (1, 4)
Comorbidities			
Charlson Comorbidity Index	1 (0, 2)	2 (1, 3)	1 (0, 2)
Atrial fibrillation	427 (39)	110 (42)	317 (38)
Arterial hypertension	775 (70)	190 (72)	585 (69)
Chronic kidney disease	252 (23)	74 (28)	178 (21)
Coronary artery disease	170 (15)	40 (15)	130 (15)
Congestive heart failure	242 (22)	55 (21)	187 (22)
Diabetes	150 (14)	31 (12)	119 (14)
Chronic lung disease	89 (8)	21 (8)	68 (8)
Respiratory support			
Invasive MV	389 (35)	97 (37)	292 (35)
Duration of MV – d	0.5 (0.18, 1.24)	0.7 (0.27, 1.38)	0.5 (0.18, 1.17)

Procedures/therapies			
Vasopressors	468 (42)	127 (48)	341 (40)
Renal replacement therapy	31 (3)	13 (5)	18 (2)
Parenteral nutrition	78 (7)	26 (10)	52 (6)
Cardiopulmonary resuscitation	82 (7)	22 (8)	60 (7)
Tracheostomy	14 (1)	4 (2)	10 (1)
Red blood cell transfusion	231 (21)	60 (23)	171 (20)
Thrombocyte transfusion	11 (1)	2 (1)	9 (1)
FFP transfusion	30 (3)	8 (3)	22 (3)
Laboratory results at admission			
Haemoglobin – g/dL	10.3 (9.2, 11.6)	10.3 (9.1, 11.5)	10.2 (9.2, 11.6)
Leukocytes – G/L	10.8 (8.0, 14.4)	10.8 (8.2, 14)	10.7 (7.8, 14.5)
Thrombocytes – G/L	208 (155, 272)	210 (159, 274)	207 (153, 269)
LDH – U/L	253 (208, 341)	252 (212, 332)	253 (107, 348)
Bilirubin – mg/dL	0.6 (0.4, 0.9)	0.6 (0.4, 0.9)	0.6 (0.4, 0.9)
CRP – mg/L	28 (8, 81)	31 (10, 82)	28 (7, 80)
Creatinine – mg/dL	1.1 (0.8, 1.6)	1.10 (0.84, 1.74)	1.10 (0.80, 1.60)
Blood gas analysis			
Lactate at admission – mmol/L	1.1 (0.8, 1.8)	1.1 (0.9, 1.9)	1.1 (0.8, 1.8)
pH at admission – level	7.37 (7.33, 7.42)	7.37 (7.31, 7.41)	7.38 (7.33, 7.42)
paO_2 at admission – mmHg	92 (74, 131)	92 (72, 131)	93 (75, 131)
pH – level, lowest/nadir	7.36 (7.29, 7.43)	7.36 (7.28, 7.43)	7.36 (7.3, 7.42)
Lactate peak – mmol/L	1.7 (1.2, 2.7)	1.9 (1.3, 2.9)	1.7 (1.1, 2.6)
Outcome			
Duration of ICU stay – d	1.6 (0.9, 3.5)	1.7 (0.9, 4.1)	1.5 (0.9, 3.2)
Duration of hospital stay – d	11 (7, 16.6)	11.1 (5.9, 17.2)	11.0 (7.0, 16.5)
Died in ICU	201 (18)	62 (23)	139 (16)
Died in hospital	331 (30)	108 (41)	223 (26)

Data are expressed as *n* (%) or median (interquartile range – IQR 25/75%). y = years; BMI = body mass index; SAPS = Simplified Acute Physiology Score; SOFA = Sequential Organ Failure Assessment; h = hours; MV = mechanical ventilation; FFP = fresh frozen plasma;

LDH = lactate dehydrogenase; CRP = C reactive protein; paO_2 = partial pressure of O_2; d = day.

Table 2. Multivariable logistic regression for factors associated with short term mortality during the hospital stay of 1 108 patients, 264 with and 844 without peripheral arterial disease (PAD), aged ≥ 90 years at a tertiary care centre in Hamburg, Germany, between 1 January 2008 and 30 April 2019.*

Variables	OR (95% CI)	*p*
PAD	1.973 (1.387–2.808)	<.001
Primary admission – elective surgery	0.648 (0.447–0.940)	.022
SAPS II at admission	1.063 (1.048–1.078)	<.001
Mechanical ventilation during ICU	2.187 (1.535–3.117)	<.001
Vasopressors during ICU	1.954 (1.363–2.802)	<.001
Higher BMI (increase by kg/m²)	0.593 (0.425–0.828)	<.001

OR = odds ratio; CI = confidence interval; PAD = peripheral arterial disease; SAPS = Simplified Acute Physiology Score; ICU = intensive care unit; BMI = body mass index; SOFA = Sequential Organ Failure Assessment.

* Variables included in the initial model: peripheral vascular disease, age, male sex, primary admission – elective surgery, SAPS II at admission, Charlson Comorbidity Index, mechanical ventilation during ICU, vasopressors during ICU, SOFA score, and BMI.

Table 3. Multivariable Cox proportional hazards model for factors associated with long term mortality of 1 108 patients, 264 with and 844 without peripheral arterial disease (PAD), aged ≥ 90 years at a tertiary care centre in Hamburg, Germany, between 1 January 2008 and 30 April 2019.*

Variables	HR (95 CI)	*p*
PAD	1.316 (1.046–1.656)	.019
Higher age (increase by 1 year)	1.040 (0.998–1.083)	.059
SAPS II at admission	1.057 (1.048–1.065)	<.001
Mechanical ventilation during ICU	1.517 (1.176–1.957)	.001

Vasopressors during ICU	1.424 (1.094–1.853)	.009

HR = hazard ratio; CI = confidence interval; PAD = peripheral arterial disease; SAPS = Simplified Acute Physiology Score; ICU = intensive care unit; BMI = body mass index; SOFA = Sequential Organ Failure Assessment.

*Variables included in the initial model: peripheral vascular disease, age, male sex, primary admission – elective surgery, SAPS II at admission, Charlson Comorbidity Index, mechanical ventilation during ICU, catecholamines during ICU, SOFA score, and BMI.

Figures

Figure 1

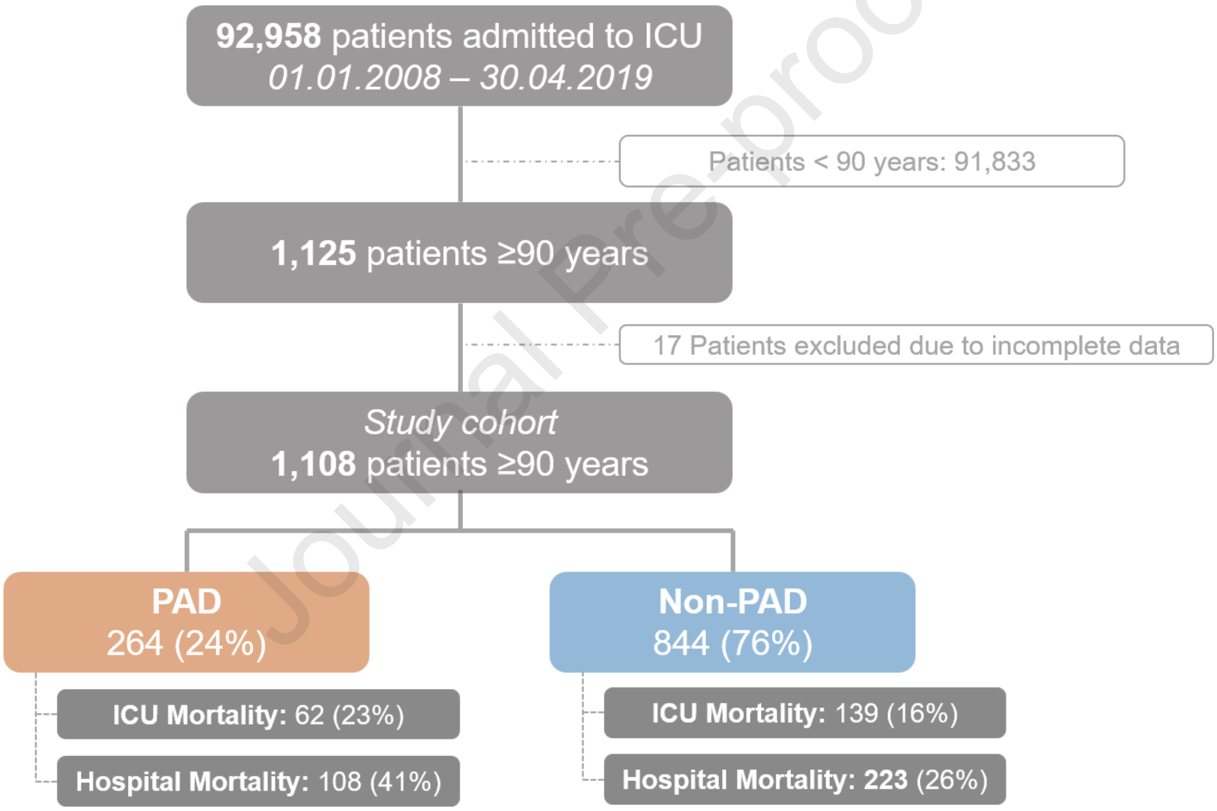
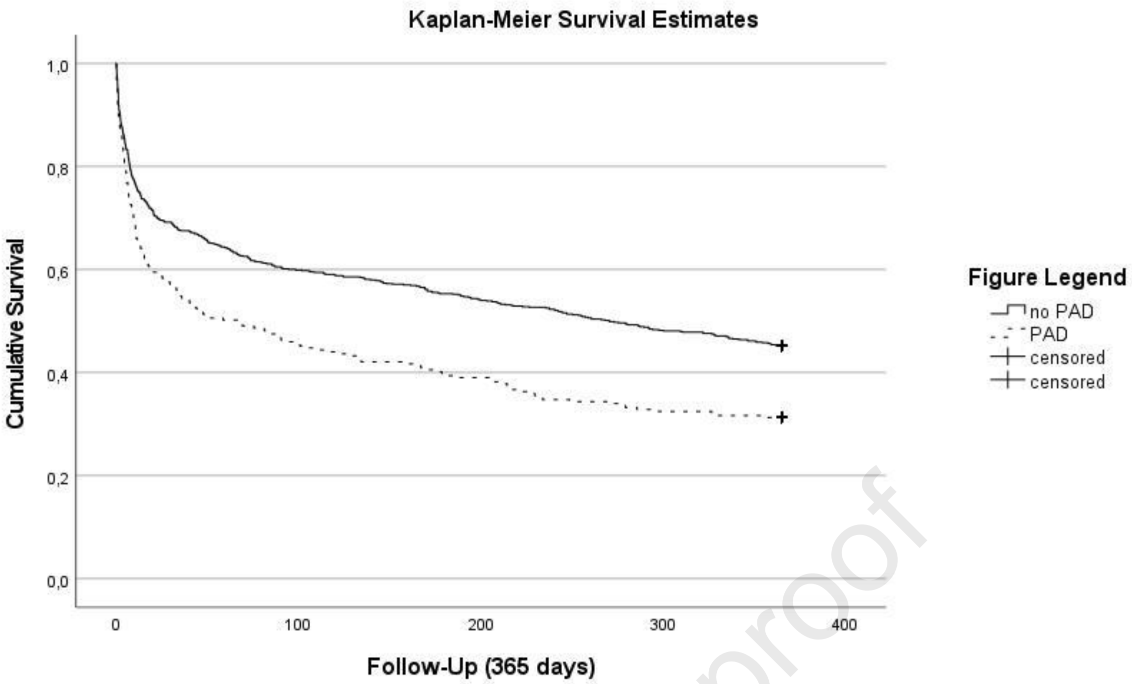


Figure 2


Kaplan-Meier Survival Estimates
Cumulative Survival
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Follow-Up (365 days)
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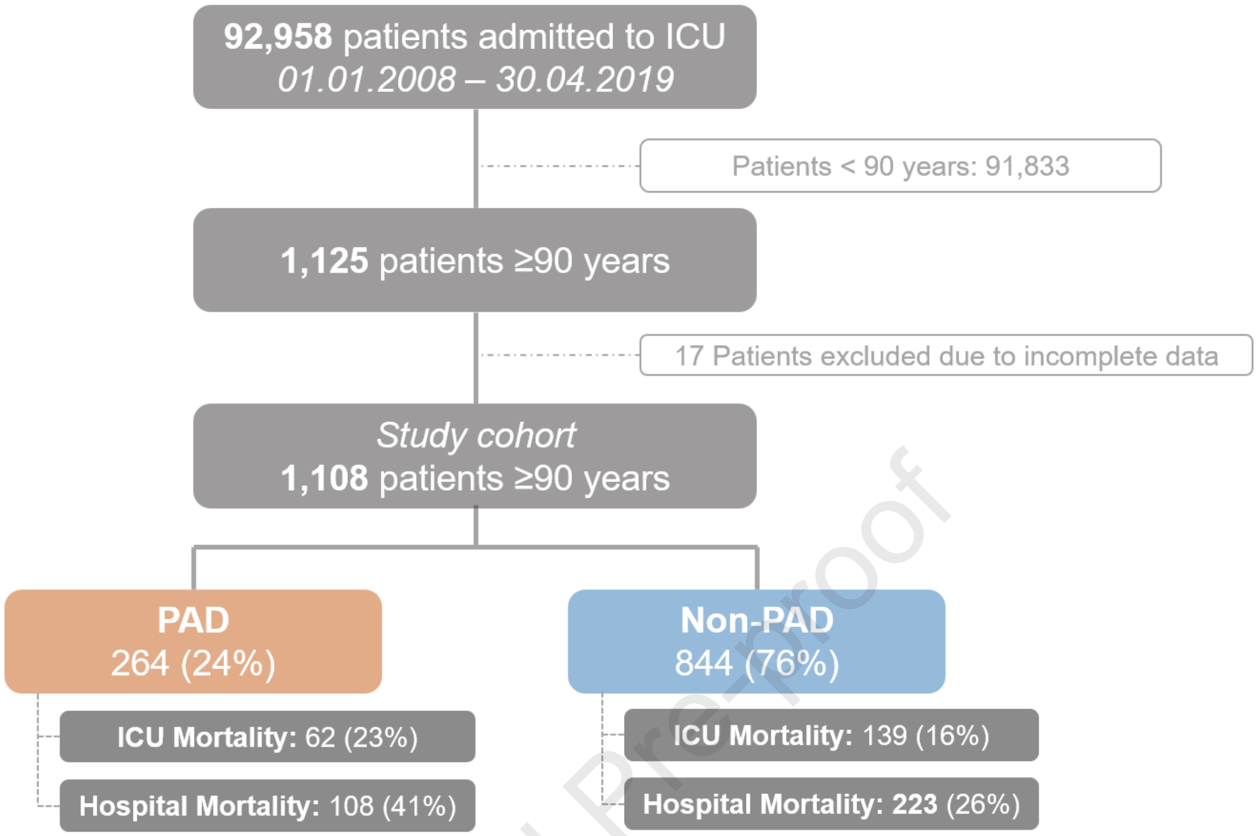
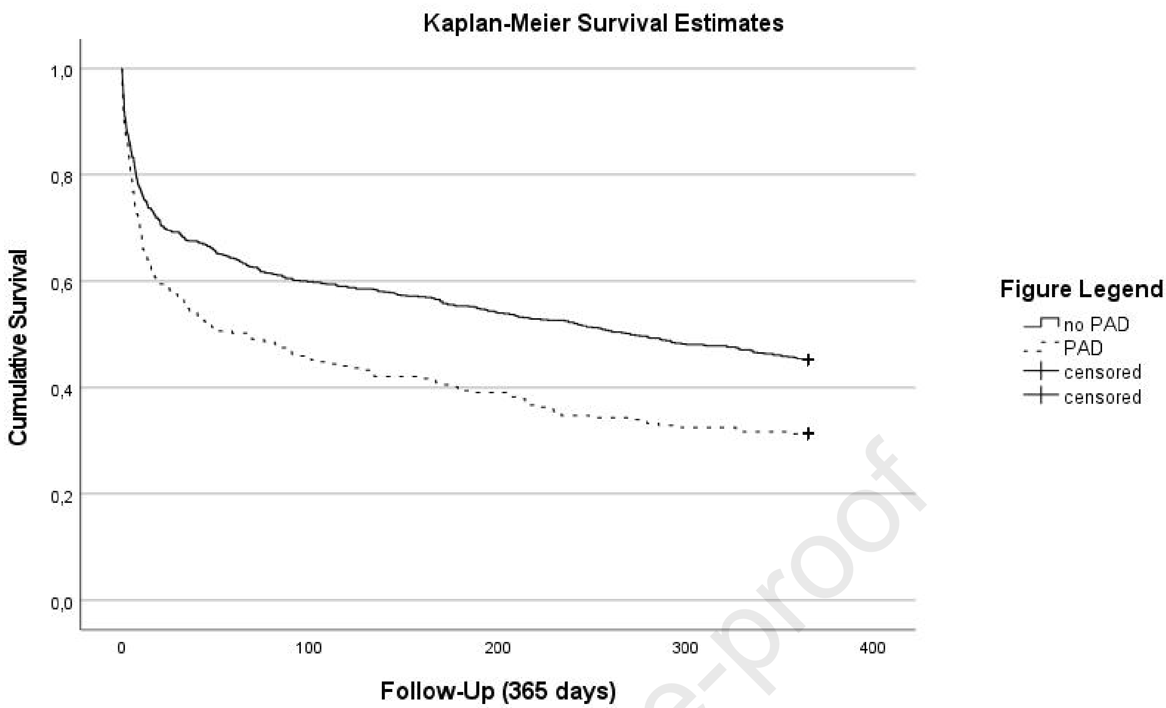

92,958 patients admitted to ICU
01.01.2008 – 30.04.2019
Patients < 90 years: 91,833
1,125 patients ≥90 years
17 Patients excluded due to incomplete data
Study cohort
1,108 patients ≥90 years
PAD
264 (24%)
ICU Mortality: 62 (23%)
Hospital Mortality: 108 (41%)
Non-PAD
844 (76%)
ICU Mortality: 139 (16%)
Hospital Mortality: 223 (26%)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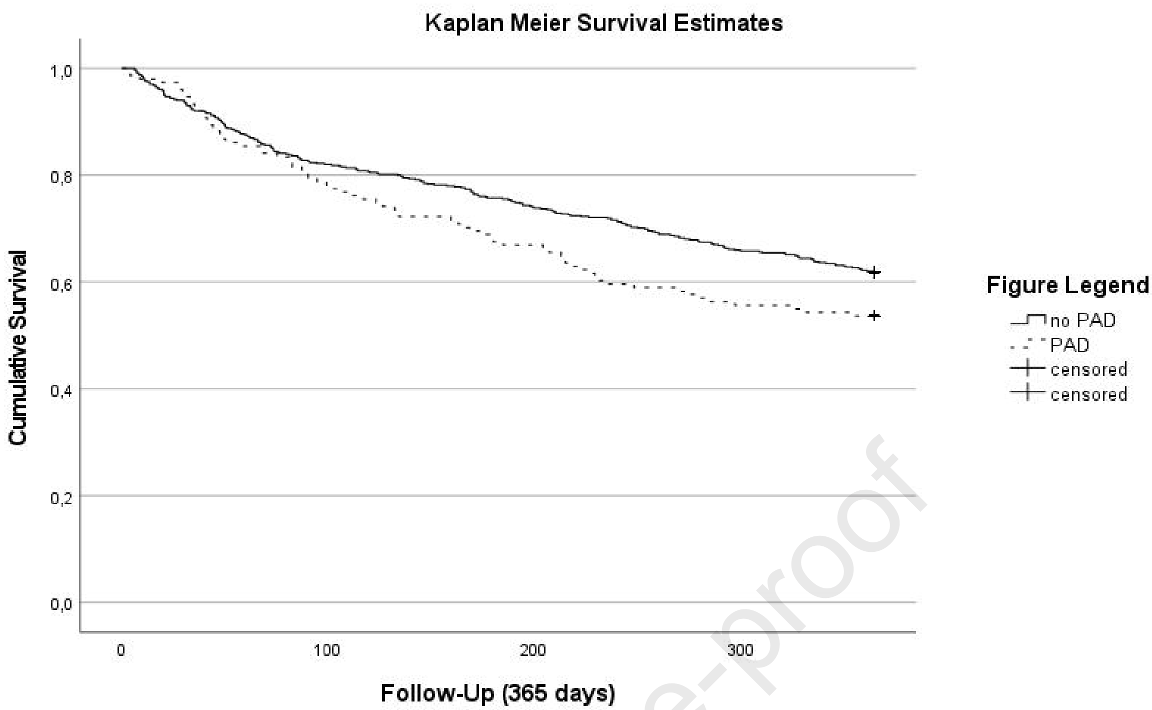
Kaplan Meier Survival Estimates
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Follow-Up (365 days)
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EJVES18282

Short title: Peripheral Vascular Disease in Patients Aged 90 Years and Older

Figures

Figure 1, delete commas in thousands, use non-breaking space instead. Flowchart - see p. C1 of the ‘EJVES instructions for typesetters’ document.

Figure 2, delete hyphen in follow up. Kaplan-Meier - see pp. H1,H2 of the ‘EJVES instructions for typesetters’ document.

Supplementary material

EJVES18282_Supplementary Fig S1 and Table S1

Supplementary Figure S1. Kaplan–Meier survival estimates landmark analysis including all patients who survived the hospital stay stratified according to the presence of peripheral arterial disease (PAD); follow up information was missing for 18 patients (2.3%).

Supplementary Table S1. Pre-existing comorbidities with and without PAD.