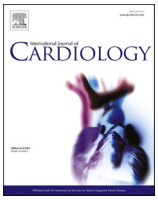
International Journal of Cardiology 442 (2026) 133898

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard



Risk factors for myocardial infarction in patients with peripheral artery disease

Karsten Keller [a,b,*], Volker H. Schmitt [a,c], Lukas Hobohm [a,b], Christine Espinola-Klein [a,b]

[a] Department of Cardiology, University Medical Center Mainz (Johannes Gutenberg-University Mainz), Mainz, Germany
[b] Center for Thrombosis and Hemostasis (CTH), University Medical Center Mainz (Johannes Gutenberg-University Mainz), Mainz, Germany
[c] German Center for Cardiovascular Research (DZHK), Partner Site Rhine Main, Mainz, Germany

ARTICLE INFO

Keywords:
Myocardial infarction
Peripheral artery disease
Pneumonia
Mortality
Diabetes mellitus

ABSTRACT

Background: Peripheral artery disease (PAD) is a worldwide major health problem characterized by a reduced blood flow in the arteries of the lower limbs due to obstructive atherosclerosis. PAD is afflicted by a high risk for adverse events of the limbs, but also by cardiovascular events such as myocardial infarction (MI).
Methods: The German nationwide inpatient statistics was used for this study. All patient-cases of patients admitted due PAD in Germany 2005–2020 were included and stratified for occurrence of MI.
Results: Overall, 2,825,765 patient-cases of patients admitted due to PAD were included in our study 2005–2020. Among these, 24,072 PAD patients (0.9 %) were afflicted by MI. PAD patients with MI were older (proportion of patients aged ≥70 years: 69.6 % vs. 54.2 %, $P < 0.001$) and revealed an aggravated comorbidity profile. In-hospital case-fatality rate was more than 10-fold increased driven by MI (29.0 % vs. 2.7 %, $P < 0.001$).
Age ≥ 70 years (OR 1.193 [95 %CI 1.158–1.229], $P < 0.001$), diabetes mellitus (OR 1.405 [95 %CI 1.369–1.442], $P < 0.001$), hyperlipidaemia (OR 1.099 [95 %CI 1.069–1.129], $P < 0.001$), COPD (OR 1.105 [95 %CI 1.064–1.148], $P < 0.001$), kidney disease (OR 1.857 [95 %CI 1.806–1.910], $P < 0.001$), heart failure (OR 4.907 [95 %CI 4.769–5.048], $P < 0.001$), atrial fibrillation/flutter (OR 1.177 [95 %CI 1.142–1.213], $P < 0.001$), cancer (OR 1.343 [95 %CI 1.242–1.451], $P < 0.001$) and pneumonia (OR 5.214 [95 %CI 5.021–5.414], $P < 0.001$) were independently associated with MI.
Conclusions: MI occurred in 0.9 % of the PAD patients and was afflicted by more than 10-fold increased case-fatality. Independent risk factors for MI events in patients admitted due to PAD comprised age ≥ 70 years, diabetes mellitus, hyperlipidaemia, lung diseases, and cancer.

1. Introduction

Peripheral artery disease (PAD) is a clinical manifestation of systemic atherosclerosis affecting the arteries, which supply the lower limbs [1,2]. More than 200 million people suffer from PAD worldwide, and the incidence is still increasing [3–5]. Pathophysiologically, the underlying atherosclerosis of PAD is shared with coronary artery disease and cerebrovascular disease [2,3]. It is increasingly acknowledged that PAD is afflicted by a high risk for adverse events of the limbs, comprising acute limb ischemia and amputation, but also by major adverse cardiovascular events such as myocardial infarction (MI) and ischaemic stroke [3,6]. Angiographic studies identified subclinical coronary artery disease in a high proportion of PAD patients undergoing vascular surgery, while approximately 30 % of these PAD patients had a severe coronary artery disease [3]. In line, clinical trials including patients with symptomatic PAD revealed a co-prevalence of known symptomatic coronary artery disease of approximately 30 % and a co-prevalence regarding history of MI of 10–20 % [3]. Although the risk for MI in PAD patients is high and PAD patients are burdened by high mortality from cardiovascular causes [6,7], the ability to predict MI is rather limited [6]. While diagnostic tools regarding predicition of MI with the use of clinical scores, myocardial scintigraphy, cardiopulmonary exercise and stress testing, computed tomography and coronary angiography among others are of outstanding importance to predict acute MI in the mid and long-term range, for short-term MI prediction and prognosis patient-characteristics might also be of outstanding value [6,8]. Most risk

* Corresponding author at: Department for Cardiology, University Medical Center Mainz, Johannes Gutenberg-University Mainz, Langenbeckstr 1, 55131 Mainz, Germany.
E-mail address: Karsten.Keller@unimedizin-mainz.de (K. Keller).

https://doi.org/10.1016/j.ijcard.2025.133898
Received 8 April 2025; Received in revised form 6 September 2025; Accepted 10 September 2025
Available online 11 September 2025

stratification models underestimate the impact of patients' comorbidities regarding outcome. However, patients'comorbidity burden often plays a crucial role in determining the in-hospital outcome of cardiovascular patients including PAD patients [4,9–12]. Thus, we aimed to identify risk factors for MI during hospitalization in PAD patients, since MI is one of the most critical events during hospitalization due to PAD and an important determining factor for survival of (hospitalized) PAD patients [4,10].

2. Methods

For this objective, we conducted an epidemiological study using the data of the German nationwide inpatient statistics including all hospitalizations of patients admitted due to PAD.

Since the year 2004, all German hospitals have to transfer their coded patient-data of hospitalizations comprising diagnoses, (coexisting) conditions/comorbidities, surgeries, interventions, treatments and procedures to the Institute for the Hospital Remuneration System and the Federal Statistical Office of Germany (Statistisches Bundesamt) to receive the remuneration for the provided/rendered patient-care services [13]. Patients' diagnoses have to be coded according to ICD-10-GM (International Classification of Diseases, 10th Revision with German Modification), while diagnostic, surgical and interventional procedures have to be coded according to the OPS-codes in order to get the remuneration (Operationen- und Prozedurenschlüssel).[30, 47]

The coding-information regarding all hospitalization-data from the inpatient cases, which is gathered by the Federal Statistical Office of Germany (Statistisches Bundesamt), is included in the German nationwide inpatient statistics (diagnosis related groups [DRG] statistic), which can be analysed for research reasons and these data are the basis of the present analysis of this study [13]. Thus, the present very large epidemiological study included all hospitalizations due to PAD during the observational period.

Our study analyses were computed by the Research Data Center (RDC) of the Federal Statistical Office and the Statistical Offices of the federal states (in Wiesbaden, Germany) on our behalf and on basis of our provided and generated SPSS syntaxes.

For the present analysis, we selected all inpatients hospitalized with a main diagnosis of PAD (ICD-code I70.2) (source: RDC of the Federal Statistical Office and the Statistical Offices of the federal states, DRG Statistics 2005–2020, own calculations) and stratified these hospitalizations for the presence of MI (ICD codes I21 and I22). Patient's main diagnosis is defined as the diagnosis, which is mainly and primarily responsible for the patient's hospitalization (and thus for admission to the hospital) [14].

2.1. Study endpoints and in-hospital adverse events

The primary study endpoint was MI during hospitalization (ICD codes I21 and I22). The second study endpoint is case-fatality rate in PAD patients with MI.

2.2. Definitions

The definition of obesity was defined according the recommendation of the WHO (World Health Organization) as body mass index ≥30 kg/m^2. Stroke comprised both stroke entities: ischaemic as well as haemorrhagic stroke. In-hospital death is defined as death from any cause during in-hospital stay and is the basis of calculated case-fatality rate.

2.3. Ethical aspects and study oversight

Since our study did not include a direct access by us (as the investigators) to individual data of patients, approval by an ethics committee and informed consent were not required, in compliance with German law. There was no commercial influence on the interpretation of the data [13].

2.4. Statistics

We compared hospitalization data of PAD patients with and without MI. Descriptive statistics for this comparison of both groups (PAD hospitalizations with and without MI) were provided with median and interquartile range (IQR), or absolute numbers and corresponding percentages and the continuous variables were compared with the help of Wilcoxon-Whitney *U* test, while the categorical variables were compared with Fisher's exact or chi [2] test, as appropriate.

Logistic regression models were used to investigate associations between patient characteristics as well as adverse in-hospital events on the one hand and occurrence of MI on the other hand. Thus, we calculated the risk for MI during in-hospital course of PAD patients. Results are presented as odds ratios (OR) and 95 % confidence intervals (CI). To ensure that the results of these logistic regressions are not biased by important comorbidities, conditions and further factors and therefore, to guarantee a wide independence, the multivariable logistic regressions were calculated with the following adjustment: age, sex, obesity, cancer, heart failure, essential arterial hypertension, hyperlipidaemia, acute and chronic kidney disease, diabetes mellitus, chronic obstructive pulmonary disease, and atrial fibrillation/flutter.

Temporal trends in the annual total numbers and proportion of PAD patients with MI among all PAD patients were analysed and illustrated.

We used the software of SPSS® (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp) for the computerised data analysis. *P* values <0.05 (two-sided) were accounted to be statistically significant.

3. Results

Overall, 2,825,765 patient-cases of patients admitted due to PAD were registered in Germany between the years 2005 and 2020 and included in our study. Among these, 24,072 PAD patients (0.9 %) were afflicted by acute MI (Table 1).

While the annual numbers of patient-cases of patients admitted due to PAD increased over the years from 2005 to 2016 and afterwards the annual numbers stagnated, before we detected an decrease in the COVID-19-pandemic year 2020, a steadily decrease regarding the occurrence of MI in these hospitalized patients was detected (Fig. 1A). We observed a rise of the patient-cases of patients admitted due to PAD in parallel with the rate of MI with increasing age (Fig. 1C).

While PAD patients with MI were older than those without (proportion of patients aged ≥70 years: 69.6 % vs. 54.2 %, $P < 0.001$), no significant difference regarding gender was identified ($P = 0.737$) (Table 1). Besides arterial hypertension, which was less commonly detected in PAD patients with MI (59.2 % vs. 63.7 %, $P < 0.001$), all other analysed traditional cardiovascular risk factors were more frequently observed in PAD patients with MI and PAD patients with MI were distinctly more often afflicted by diabetes mellitus (47.1 % vs. 32.6 %, $P < 0.001$) (Table 1).

PAD patients with MI revealed an aggravated comorbidity burden with higher rates of cardiac diseases, such as heart failure (48.8 % vs. 12.2 %, $P < 0.001$) and atrial fibrillation/flutter (30.1 % vs. 15.1 %, $P < 0.001$), but also pulmonary and renal disease including chronic obstructive pulmonary disease (COPD) (13.5 % vs. 9.2 %, $P < 0.001$) as well as acute and chronic kidney disease (52.2 % vs. 25.4 %, $P < 0.001$) (Table 1). Interestingly, also cancer (2.8 % vs. 1.8 %, $P < 0.001$) was more often found in PAD patients with MI.

All investigated adverse in-hospital events occurred more frequently in PAD patients with than without MI (Table 1). In this context, in-hospital case-fatality rate was more than 10-fold increased driven by MI (29.0 % vs. 2.7 %, $P < 0.001$). Although the annual case-fatality decreased steadily from 2005 to 2020 (Fig. 1C), the case-fatality increased remarkably with age (Fig. 1D).

Table 1
Patients' characteristics, medical history, presentation and outcomes of the included 2,825,765 patient-cases of patients admitted due to peripheral artery disease (PAD) stratified for occurrence of myocardial infarction (MI).

Parameters	PAD patients without MI (n = 2,801,693; 99.1 %)	PAD patients with MI (n = 24,072; 0.9 %)	P-value
Age ≥ 70 years	1,519,749 (54.2 %)	16,745 (69.6 %)	**<0.001**
Female sex	1,029,208 (36.7 %)	8817 (36.6 %)	0.737
Traditional cardiovascular risk factors			
Essential arterial hypertension	1,783,938 (63.7 %)	14,257 (59.2 %)	**<0.001**
Diabetes mellitus	913,889 (32.6 %)	11,339 (47.1 %)	**<0.001**
Hyperlipidaemia	995,806 (35.5 %)	8880 (36.9 %)	**<0.001**
Obesity	212,638 (7.6 %)	1915 (8.0 %)	**0.033**
Comorbidities			
Heart failure	342,288 (12.2 %)	11,744 (48.8 %)	**<0.001**
Atrial fibrillation/flutter	422,463 (15.1 %)	7254 (30.1 %)	**<0.001**
Chronic obstructive pulmonary disease	257,486 (9.2 %)	3244 (13.5 %)	**<0.001**
Acute and chronic kidney disease	711,542 (25.4 %)	12,573 (52.2 %)	**<0.001**
Cancer	49,429 (1.8 %)	678 (2.8 %)	**<0.001**
Adverse events during hospitalization			
In-hospital death	74,334 (2.7 %)	6985 (29.0 %)	**<0.001**
Cardio-pulmonary resuscitation	14,437 (0.5 %)	3411 (14.2 %)	**<0.001**
Shock	18,231 (0.7 %)	3092 (12.8 %)	**<0.001**
Aorto-coronary bypass graft	356 (0.01 %)	190 (0.8 %)	**<0.001**
Pneumonia	47,287 (1.7 %)	3977 (16.5 %)	**<0.001**
Deep venous thrombosis and/or thrombophlebitis	14,337 (0.5 %)	232 (1.0 %)	**<0.001**
Pulmonary embolism	3234 (0.1 %)	173 (0.7 %)	**<0.001**
Acute kidney injury	51,897 (1.9 %)	3549 (14.7 %)	**<0.001**
Stroke (ischaemic or haemorrhagic)	13,068 (0.5 %)	700 (2.9 %)	**<0.001**
Intracerebral bleeding	845 (0.03 %)	37 (0.2 %)	**<0.001**
Gastrointestinal bleeding	11,532 (0.4 %)	577 (2.4 %)	**<0.001**
Transfusion of blood constituents	291,716 (10.4 %)	11,747 (48.8 %)	**<0.001**

In line, cardio-pulmonary resuscitation, shock and pneumonia were about 10-fold more prevalent in PAD patients with MI. In addition, stroke occurred approximately 6-fold as often in patients with than without MI. Nearby half of the PAD patients with MI required a transfusion of blood constituents (Table 1).

The frequency of MI increased from 3.7 % in PAD stage I regarding Fontaine classification to 6.1 % in stage IV (Fig. 2A). In PAD patients with MI, the in-hospital case-fatality was high with 30.0 % in PAD stage I regarding Fontaine classification and inclined to 50.8 % in stage III and 49.2 % in stage IV (Fig. 2B).Independent risk factors for MI events in patients admitted due to PAD comprised age ≥ 70 years (OR 1.193 [95 %CI 1.158–1.229], $P < 0.001$), diabetes mellitus (OR 1.405 [95 %CI 1.369–1.442], $P < 0.001$) and hyperlipidaemia (OR 1.099 [95 %CI 1.069–1.129], $P < 0.001$) (Table 2). Among cardiac comorbidities, heart failure (OR 4.907 [95 %CI 4.769–5.048], $P < 0.001$) and atrial fibrillation/flutter (OR 1.177 [95 %CI 1.142–1.213], $P < 0.001$) were independently associated with MI events. In addition, COPD (OR 1.105 [95 %CI 1.064–1.148], $P < 0.001$), acute and chronic kidney disease (OR 1.857 [95 %CI 1.806–1.910], $P < 0.001$), cancer (OR 1.343 [95 %CI 1.242–1.451], $P < 0.001$) as well as pneumonia (OR 5.214 [95 %CI 5.021–5.414], $P < 0.001$) and pulmonary embolism (OR 3.536 [95 %CI 3.020–4.140], $P < 0.001$) were related to MI (Table 2).

In addition, an increase in PAD stage regarding Fontaine classification (OR 1.081 [95 %CI 1.030–1.134], $P < 0.001$) was associated with MI occurrence, but after adjustment for age, sex and comorbidities this association did not remain significant (OR 1.040 [95 %CI 0.992–1.091], $P = 0.106$).

It is important that MI was only in some of the PAD stages of Fontaine classification independently associated with case-fatality. While MI was not significantly and independently related to case-fatality in stage I (OR 1.806 [95 %CI 0.369–8.836], $P = 0.465$), in stage IIa (OR 4.158 [95 %CI 2.466–7.009], $P < 0.001$), stage IIb (OR 3.197 [95 %CI 2.184–4.679], $P < 0.001$), stage III (OR 1.970 [95 %CI 1.548–2.506], $P < 0.001$) and stage IV (OR 1.840 [95 %CI 1.233–2.747], $P = 0.003$) MI was independently of age, sex and comorbidities associated with increased case-fatality.

4. Discussion

Peripheral artery disease (PAD) is a worldwide major health problem characterized by a reduced blood flow in the arteries of the lower limbs due to obstructive atherosclerosis [15]. Our study, including almost 3 million patient-cases of patients who were admitted to German hospitals during the years between 2005 and 2020 underline the scope of the problem in western countries and worldwide. As reported by epidemiological studies, the prevalence of PAD increased with age also in our study [5,16].

MI is a devastating event during the hospitalization course of PAD patients [4,6,7,10]. Although the annual case-fatality decreased steadily from 2005 to 2020, our study demonstrated that MI events were still afflicted with a more than 10-fold increased case-fatality in PAD patients. In addition, case-fatality increased substantially with age. It is well established that patients with large-vessel PAD have a high risk to die from cardiovascular causes [7,15,17]. Studies reported a mortality rate of PAD patients ranging between 24.6 and 25.5 % after 2.5 years follow-up [15]. In long-term, 61.8 % of the male and 33.3 % of the female PAD patients died during a 10-years follow-up [7]. PAD patients are accompanied by a 4.5-fold increased relative risk of death in comparison to age-matched patients without PAD [7]. For patients with symptomatic PAD, the 10-year risk of death due to coronary artery disease or cardiovascular disease was 10–15-fold elevated compared to subjects who were free of PAD [7]. This association of PAD with increased mortality was independent of other risk factors for cardiovascular disease and also independent of the presence of cardiovascular diseases at baseline [7,15]. Atherosclerotic involvement of more than one arterial bed results in the worst prognosis [2,18]. Contrariwise, PAD influences the outcome of MI patients negatively [19–21].

Driven by this crucial and important impact of MI on PAD patients' survival, it is of outstanding interest to optimize patient care with improved management of patients suffering from PAD to prevent MI and death during hospitalization and afterwards [18]. However, approximately 1 % of the hospitalized PAD patients in Germany included in our study were afflicted by an acute MI 2005–2020. Studies revealed an increased risk for MI in PAD patients; the relative risk was 1.67 (95 %CI: 1.05–2.66) compared to the participants without PAD [2]. In mid- and long-term studies MI was observed in 4.0–4.6 % of all PAD patients after a median follow-up period of 28 months follow-up[3] and in other studies 4.8–5.0 % after a median follow-up of 30 months [1,22].

Stroke events occurred in our study in 0.5 % of the PAD patients without MI and in 2.9 % of the PAD patients with MI. In accordance, incidence of stroke was reported between 1.9 % and 2.4 % in symptomatic PAD patients after a median follow-up of 30 month [1].

In accordance with studies regarding risk factors for MI in the general population, increased age as well as the cardiovascular risk factors diabetes mellitus, and hyperlipidaemia were independently associated with increased risk for MI incidence [23–25]. In contrast to previously published studies, arterial hypertension was in our study not associated with an increased risk for MI [24–26].

In addition, higher PAD stage according Fontaine classification was also associated with increased MI rate, but this association was

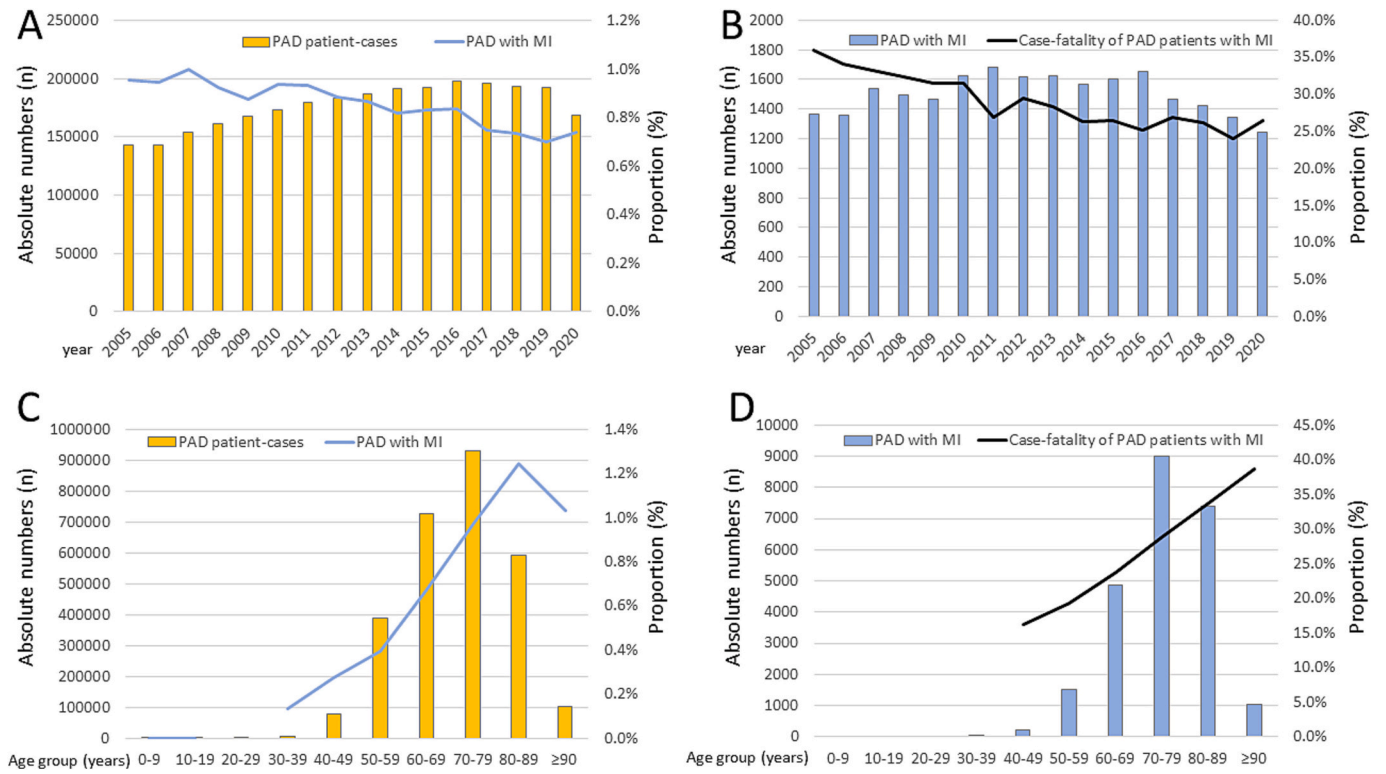


Fig. 1. Time trends of hospitalized patients with peripheral artery disease (PAD) and concomitant myocardial infarction (MI).
Panel A: Annual time trend regarding absolute numbers of PAD patients and occurrence of MI in these patients during the timeframe of the years 2005–2020.
Panel B: Annual time trend regarding absolute numbers of PAD patients with MI and their case-fatality rate during the timeframe of the years 2005–2020.
Panel C: Age-dependent trend regarding absolute numbers of PAD patients and occurrence of MI in these patients during the timeframe of the years 2005–2020 in the different age-decades.
Panel D Age-dependent trend regarding absolute numbers of PAD patients with MI and their case-fatality rate during the timeframe of the years 2005–2020 in the different age-decades.

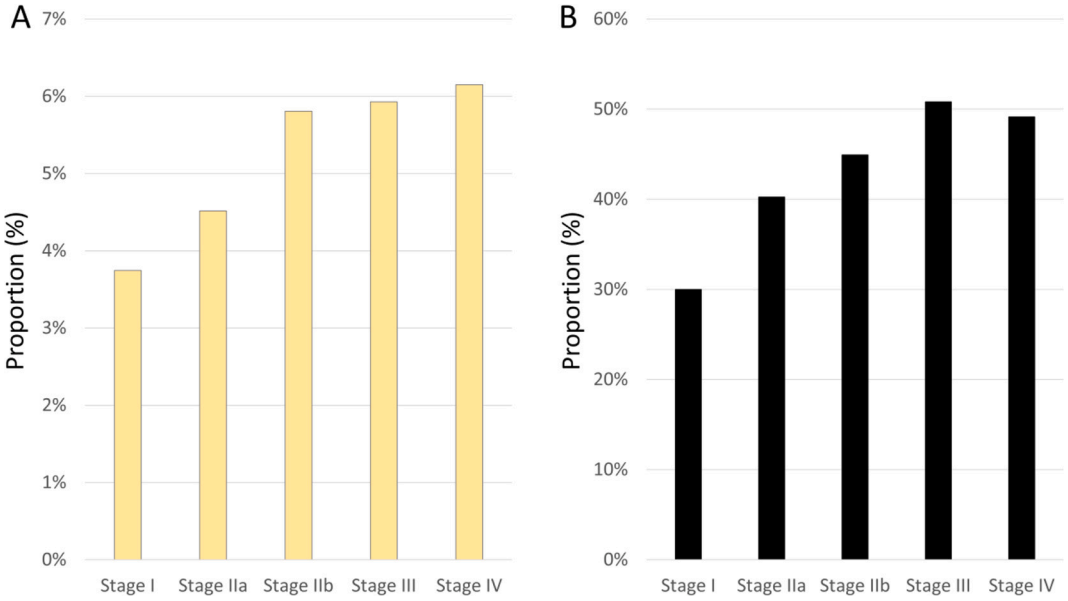


Fig. 2. MI frequency (A) in PAD hospitalizations and case-fatality in PAD patieents with MI (B) stratified by PAD stages regarding Fontaine classification.

influenced by age, sex and comorbidities.

Among cardiovascular comorbidities, heart failure and atrial fibrillation/flutter were independently associated with MI events, whereby it is not clear if these cardiovascular comorbidities occurred as a result of MI or were already present before MI in the baseline characteristics of the included PAD patients [23,27]. In addition, also pulmonary diseases such as COPD, pneumonia and pulmonary embolism were related to MI. In this context, several studies have suggested an increased risk for acute MI in patients with pneumonia [28–30]. The 90-day incidence of MI was 1.5 % in a large study comprising more than 50,000 patients who were

Table 2
Risk factors for myocardial infarction in hospitalized patients admitted due to peripheral artery disease (univariable and multivariable logistic regression models).

	Univariable regression model		Multivariable regression model*	
	OR (95 % CI)	P-value	OR (95 % CI)	P-value
Age ≥ 70 years	1.928 (1.875–1.982)	**<0.001**	1.193 (1.158–1.229)	**<0.001**
Female sex	0.996 (0.970–1.022)	0.737	0.904 (0.880–0.930)	**<0.001**
Traditional cardiovascular risk factors				
Essential arterial hypertension	0.829 (0.808–0.850)	**<0.001**	0.923 (0.899–0.948)	**<0.001**
Diabetes mellitus	1.840 (1.793–1.887)	**<0.001**	1.405 (1.369–1.442)	**<0.001**
Hyperlipidaemia	1.060 (1.033–1.088)	**<0.001**	1.099 (1.069–1.129)	**<0.001**
Obesity	1.052 (1.004–1.103)	**0.033**	0.869 (0.828–0.911)	**<0.001**
Comorbidities				
Heart failure	6.845 (6.672–7.022)	**<0.001**	4.907 (4.769–5.048)	**<0.001**
Atrial fibrillation/ flutter	2.429 (2.363–2.497)	**<0.001**	1.177 (1.142–1.213)	**<0.001**
Chronic obstructive pulmonary disease	1.539 (1.483–1.597)	**<0.001**	1.105 (1.064–1.148)	**<0.001**
Acute and chronic kidney disease	3.212 (3.131–3.295)	**<0.001**	1.857 (1.806–1.910)	**<0.001**
Cancer	1.614 (1.494–1.743)	**<0.001**	1.343 (1.242–1.451)	**<0.001**
Pneumonia	11.528 (11.129–11.941)	**<0.001**	5.214 (5.021–5.414)	**<0.001**
Pulmonary embolism	6.264 (5.373–7.303)	**<0.001**	3.536 (3.020–4.140)	**<0.001**

* Adjusted for age, sex, obesity, cancer, heart failure, essential arterial hypertension, hyperlipidemia, acute and chronic kidney disease, diabetes mellitus, chronic obstructive pulmonary disease, and atrial fibrillation/flutter.

at least 65 years old [28]. Also COPD is strongly associated with increased incidence of MI [30,31]. Besides shared cardiovascular risk factors, specific COPD-related factors, such as systemic inflammation, but also hypoxia, are pathophysiologically involved in the interaction between COPD and MI originating in atherosclerosis and increasing thrombogenic factors [31]. Furthermore, high- and intermediate-high-risk PE share similarities with acute MI events [32]. While in MI an early reperfusion therapy is aimed to restore coronary artery blood flow and to prevent myocardial necrosis as well as decrease of the left ventricular systolic function, in high- and intermediate-high-risk PE patients reperfusion therapy targets to restore pulmonary blood flow, to improve gas exchange, and to prevent/improve and alleviate right ventricular dysfunction [32,33].

Studies revealed that even a moderate renal failure was accompanied with an increased risk of MI independent of clinical variables, baseline angiographic evidence of coronary disease and therapy [34,35]. In addition, patients with renal failure bear an increased risk for death after acute MI; this might be in part explained by receiving less aggressive treatment than patients with normal renal function [36]. Our study results demonstrated a strong association between acute and chronic kidney disease and MI.

In literature, cancer as an important comorbid condition in MI patients is strongly associated with mortality, severe bleeding, and adverse cardiovascular outcome after first MI [37]. In the included PAD patients of the German nationwide inpatient statistics of our study, cancer was associated with an increased risk for MI. Furthermore, individuals with cardiovascular diseases such as MI have an elevated risk regarding developing cancer [38]. The association regarding the relation between cancer and atherosclerosis might be in part driven by specific cancer subtypes promoting atherosclerosis and therefore favour the development of atherosclerotic diseases such as PAD and MI [38].

Condensed, the results of our study emphasize the necessity for an optimized management of the comorbid profile and the cardiovascular risk factors to prevent acute MI in PAD patients. In this context, the prognosis of PAD patients can be substantially improved by secondary preventive measures including strict lifestyle modification and medical control of all modifiable cardiovascular risk factors [2,18,23,39].

5. Limitations

The following limitations of our study merit consideration: Firstly, due to the nature of ICD- and OPS-code-based study-analysis of hospitalized patients of the German nationwide-inpatient statistics, underreporting as well as under-coding are possible. Secondly, data on most concomitant medications as well as data on laboratory markers are not available. Thirdly, the data of the German nationwide statistics includes only data about the hospitalization duration, but no follow-up evaluation after discharge from the hospital.

6. Conclusions

MI events occurred in 0.9 % of the patient-cases of patients admitted to a hospital due to PAD and were afflicted by a more than 10-fold increased case-fatality in PAD patients. Independent risk factors for MI events in patients admitted due to PAD comprised age ≥ 70 years, diabetes mellitus, hyperlipidaemia, acute and chronic lung diseases, cancer and kidney disease. Among cardiac comorbidities, heart failure and atrial fibrillation/flutter were independently associated with MI events.

7. Lay summary

- In the large German nationwide inpatient statistics involving 2,825,765 patient-cases of patients admitted due to PAD, we detected an MI incidence of nearby 1 %.
- Independent risk factors for MI events in patients admitted due to PAD comprised age ≥ 70 years, diabetes mellitus, hyperlipidaemia, lung diseases, and cancer and MI was afflicted by approxiamtely 10-fold case-fatality risk in PAD patiet-cases.
- These study-results emphasize the necessity for an optimized management of the comorbid profile and the cardiovascular risk factors to prevent acute MI in PAD patients.

CRediT authorship contribution statement

Karsten Keller: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Volker H. Schmitt:** Writing – review & editing. **Lukas Hobohm:** Writing – review & editing, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Christine Espinola-Klein:** Writing – review & editing.

Declaration of competing interest

KK and VHS report no conflict of interests. LH received lecture/consultant fees from MSD, Boston Scientific and Inari Medical, outside the submitted work. CEK reports having from Amarin Germany, Amgen GmbH, Bayer Vital, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Leo Pharma, MSD Sharp & Dohme, Novartis Pharma, Pfizer Pharma GmbH, Sanofi-Aventis GmbH, outside the submitted work.

Data availability

All codes used in this study are publicly available online. The data/results are available at the Federal Statistical Office of Germany (Statistisches Bundesamt, DEStatis) (source: RDC of the Federal Statistical Office and the Statistical Offices of the federal states, DRG Statistics 2005–2020, and own calculations).

References

[1] W.R. Hiatt, F.G. Fowkes, G. Heizer, J.S. Berger, I. Baumgartner, P. Held, B. G. Katona, K.W. Mahaffey, L. Norgren, W.S. Jones, J. Blomster, M. Millegard, C. Reist, M.R. Patel, E.T.S. Committee, Investigators., Ticagrelor versus Clopidogrel in symptomatic peripheral artery disease, N. Engl. J. Med. 376 (2017) 32–40.

[2] E.L. Perez Mejias, S.M. Faxas, N.T. Taveras, A.S. Talpur, J. Kumar, M. Khalid, S. K. Aruwani, D. Khalid, H. Khalid, S. Memon, Peripheral artery disease as a risk factor for myocardial infarction, Cureus 13 (2021) e15655.

[3] M.P. Bonaca, R.M. Bauersachs, S.S. Anand, E.S. Debus, M.R. Nehler, M.R. Patel, F. Fanelli, W.H. Capell, L. Diao, N. Jaeger, C.N. Hess, A.F. Pap, J.M. Kittelson, I. Gudz, L. Matyas, D.K. Krievins, R. Diaz, M. Brodmann, E. Muehlhofer, L. P. Haskell, S.D. Berkowitz, W.R. Hiatt, Rivaroxaban in peripheral artery disease after revascularization, N. Engl. J. Med. 382 (2020) 1994–2004.

[4] A. Kochar, H. Mulder, F.W. Rockhold, I. Baumgartner, J.S. Berger, J.I. Blomster, F. G.R. Fowkes, B.G. Katona, R.D. Lopes, H.R. Al-Khalidi, K.W. Mahaffey, L. Norgren, W.R. Hiatt, M.R. Patel, W.S. Jones, Cause of death among patients with peripheral artery disease: insights from the EUCLID trial, Circ. Cardiovasc. Qual. Outcomes 13 (2020) e006550.

[5] A.W. Aday, K. Matsushita, Epidemiology of peripheral artery disease and polyvascular disease, Circ. Res. 128 (2021) 1818–1832.

[6] E. Rossi, L.M. Biasucci, F. Citterio, S. Pelliccioni, C. Monaco, F. Ginnetti, D. J. Angiolillo, G. Grieco, G. Liuzzo, A. Maseri, Risk of myocardial infarction and angina in patients with severe peripheral vascular disease: predictive role of C-reactive protein, Circulation 105 (2002) 800–803.

[7] M.H. Criqui, R.D. Langer, A. Fronek, H.S. Feigelson, M.R. Klauber, T.J. McCann, D. Browner, Mortality over a period of 10 years in patients with peripheral arterial disease, N. Engl. J. Med. 326 (1992) 381–386.

[8] H.H. Feringa, J.J. Bax, S. Hoeks, V.H. van Waning, A. Elhendy, S. Karagiannis, R. Vidakovic, O. Schouten, E. Boersma, D. Poldermans, A prognostic risk index for long-term mortality in patients with peripheral arterial disease, Arch. Intern. Med. 167 (2007) 2482–2489.

[9] K. Keller, L. Hobohm, T. Munzel, M.A. Ostad, C. Espinola-Klein, Impact of chronic obstructive pulmonary disease on the outcomes of patients with peripheral artery disease, Respir. Med. 147 (2019) 1–6.

[10] F. Sartipy, B. Sigvant, F. Lundin, E. Wahlberg, Ten year mortality in different peripheral arterial disease stages: a population based observational study on outcome, Eur. J. Vasc. Endovasc. Surg. 55 (2018) 529–536.

[11] K. Keller, V.H. Schmitt, O. Hahad, C. Espinola-Klein, T. Munzel, P. Lurz, S. Konstantinides, L. Hobohm, Categorization of patients with pulmonary embolism by Charlson comorbidity index, Am J Med. 137 (8) (2024 Aug) 727–735, https://doi.org/10.1016/j.amjmed.2024.04.025. Epub 2024 Apr 24.

[12] K. Keller, L. Hobohm, M. Geyer, T. Munzel, C.J. Lavie, M.A. Ostad, C. Espinola-Klein, Obesity paradox in peripheral artery disease, Clin. Nutr. 38 (2019) 2269–2276.

[13] K. Keller, L. Hobohm, M. Ebner, K.P. Kresoja, T. Munzel, S.V. Konstantinides, M. Lankeit, Trends in thrombolytic treatment and outcomes of acute pulmonary embolism in Germany, Eur. Heart J. 41 (2020) 522–529.

[14] Internet page of the InEK GmbH – Institut für das Entgeltsystem im Krankenhaus vanO. Deutsche Kodierrichtlinien 2018 Druckversion A4 (PDF). https://wwwg-drgde/inek_site_de/layout/set/standard/Media/Files/G-DRG-System/G-DRG-System_2018/Deutsche_Kodierrichtlinien_2018_Druckversion_A4_PDF, 2018.

[15] J. Nordanstig, S. James, M. Andersson, M. Andersson, P. Danielsson, P. Gillgren, M. Delle, J. Engstrom, T. Fransson, M. Hamoud, A. Hilbertson, P. Johansson, L. Karlsson, B. Kragsterman, H. Lindgren, K. Ludwigs, S. Mellander, N. Nyman, H. Renlund, B. Sigvant, P. Skoog, J. Starck, G. Tegler, A. Toivola, M. Truedson, C. M. Wahlgren, J. Wallinder, A. Ojersjo, M. Falkenberg, Mortality with paclitaxel-coated devices in peripheral artery disease, N. Engl. J. Med. 383 (2020) 2538–2546.

[16] M.H. Criqui, V. Aboyans, Epidemiology of peripheral artery disease, Circ. Res. 116 (2015) 1509–1526.

[17] N. Malyar, T. Furstenberg, J. Wellmann, M. Meyborg, F. Luders, K. Gebauer, H. Bunzemeier, N. Roeder, H. Reinecke, Recent trends in morbidity and in-hospital outcomes of in-patients with peripheral arterial disease: a nationwide population-based analysis, Eur. Heart J. 34 (2013) 2706–2714.

[18] P.G. Steg, D.L. Bhatt, P.W. Wilson, R. D'Agostino Sr., E.M. Ohman, J. Rother, C. S. Liau, A.T. Hirsch, J.L. Mas, Y. Ikeda, M.J. Pencina, S. Goto, R.R. Investigators, One-year cardiovascular event rates in outpatients with atherothrombosis, JAMA 297 (2007) 1197–1206.

[19] E. Freisinger, N.M. Malyar, H. Reinecke, Peripheral artery disease is associated with high in-hospital mortality particularly in males with acute myocardial infarction in a nationwide real-world setting, Vasa 45 (2016) 169–174.

[20] A. Jeremias, L. Gruberg, J. Patel, G. Connors, D.L. Brown, Effect of peripheral arterial disease on in-hospital outcomes after primary percutaneous coronary intervention for acute myocardial infarction, Am. J. Cardiol. 105 (2010) 1268–1271.

[21] I. Kirchberger, U. Amann, M. Heier, B. Kuch, C. Thilo, A. Peters, C. Meisinger, Presenting symptoms, pre-hospital delay time and 28-day case fatality in patients with peripheral arterial disease and acute myocardial infarction from the MONICA/KORA myocardial infarction registry, Eur. J. Prev. Cardiol. 24 (2017) 265–273.

[22] C.B. Olivier, H. Mulder, W.R. Hiatt, W.S. Jones, F.G.R. Fowkes, F.W. Rockhold, J. S. Berger, I. Baumgartner, P. Held, B.G. Katona, L. Norgren, J. Blomster, M.R. Patel, K.W. Mahaffey, Incidence, characteristics, and outcomes of myocardial infarction in patients with peripheral artery disease: insights from the EUCLID trial, JAMA Cardiol. 4 (2019) 7–15.

[23] R.A. Byrne, X. Rossello, J.J. Coughlan, E. Barbato, C. Berry, A. Chieffo, M.J. Claeys, G.A. Dan, M.R. Dweck, M. Galbraith, M. Gilard, L. Hinterbuchner, E.A. Jankowska, P. Juni, T. Kimura, V. Kunadian, M. Leosdottir, R. Lorusso, Pedretti RFE, A. G. Rigopoulos, M. Rubini Gimenez, H. Thiele, P. Vranckx, S. Wassmann, N. K. Wenger, B. Ibanez, Group ESCSD, ESC guidelines for the management of acute coronary syndromes, Eur. Heart J. 2023 (44) (2023) 3720–3826.

[24] S. Yusuf, S. Hawken, S. Ounpuu, T. Dans, A. Avezum, F. Lanas, M. McQueen, A. Budaj, P. Pais, J. Varigos, L. Lisheng, I.S. Investigators, Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study, Lancet 364 (2004) 937–952.

[25] M.A. Salinero-Fort, F.J.S. Andres-Rebollo, J. Cardenas-Valladolid, M. Mendez-Bailon, R.M. Chico-Moraleja, E.C. de Santa Pau, I. Jimenez-Trujillo, I. Gomez-Campelo, Lunar C. de Burgos, J.M. de Miguel-Yanes, Madiabetes, Cardiovascular risk factors associated with acute myocardial infarction and stroke in the MADIABETES cohort, Sci. Rep. 11 (2021) 15245.

[26] M. Sakalaki, A. Pivodic, K. Svardsudd, P.O. Hansson, M. Fu, Cumulative incidence and risk factors of myocardial infarction during 20 years of follow-up: comparing two cohorts of middle-aged men born 30 years apart, Clin. Res. Cardiol. 113 (2024) 1661–1669.

[27] F. Violi, E.Z. Soliman, P. Pignatelli, D. Pastori, Atrial fibrillation and myocardial infarction: a systematic review and appraisal of pathophysiologic mechanisms, J. Am. Heart Assoc. (2016) 5.

[28] T.W. Perry, M.J. Pugh, G.W. Waterer, B. Nakashima, C.J. Orihuela, L.A. Copeland, M.I. Restrepo, A. Anzueto, E.M. Mortensen, Incidence of cardiovascular events after hospital admission for pneumonia, Am. J. Med. 124 (2011) 244–251.

[29] J. Ramirez, S. Aliberti, M. Mirsaeidi, P. Peyrani, G. Filardo, A. Amir, B. Moffett, J. Gordon, F. Blasi, J. Bordon, Acute myocardial infarction in hospitalized patients with community-acquired pneumonia, Clin. Infect. Dis. 47 (2008) 182–187.

[30] D.M. Musher, M.S. Abers, V.F. Corrales-Medina, Acute infection and myocardial infarction, Reply. N Engl J Med. 380 (2019) e21.

[31] L. Goedemans, J.J. Bax, V. Delgado, COPD and acute myocardial infarction, Eur. Respir. Rev. 29 (2020).

[32] M. Zuin, G. Piazza, Is it time for a myocardial infarction approach to high- and intermediate-high-risk pulmonary embolism? EuroIntervention 20 (2024) e1129–e1131.

[33] S.V. Konstantinides, G. Meyer, C. Becattini, H. Bueno, G.J. Geersing, V.P. Harjola, M.V. Huisman, M. Humbert, C.S. Jennings, D. Jimenez, N. Kucher, I.M. Lang, M. Lankeit, R. Lorusso, L. Mazzolai, N. Meneveau, F.N. Ainle, P. Prandoni, P. Pruszczyk, M. Righini, A. Torbicki, E. Van Belle, J.L. Zamorano, The Task Force for the d and management of acute pulmonary embolism of the European Society of C. 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): the task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC), Eur. Respir. J. (2019) 54.

[34] S. Beddhu, K. Allen-Brady, A.K. Cheung, B.D. Horne, T. Bair, J.B. Muhlestein, J. L. Anderson, Impact of renal failure on the risk of myocardial infarction and death, Kidney Int. 62 (2002) 1776–1783.

[35] C. Meisinger, A. Doring, H. Lowel, Group KS, Chronic kidney disease and risk of incident myocardial infarction and all-cause and cardiovascular disease mortality in middle-aged men and women from the general population, Eur. Heart J. 27 (2006) 1245–1250.

[36] R.S. Wright, G.S. Reeder, C.A. Herzog, R.C. Albright, B.A. Williams, D.L. Dvorak, W.L. Miller, J.G. Murphy, S.L. Kopecky, A.S. Jaffe, Acute myocardial infarction and renal dysfunction: a high-risk combination, Ann. Intern. Med. 137 (2002) 563–570.

[37] M.A. Velders, E. Hagstrom, S.K. James, Temporal trends in the prevalence of Cancer and its impact on outcome in patients with first myocardial infarction: a Nationwide study, J. Am. Heart Assoc. 9 (2020) e014383.

[38] C.F. Bell, X. Lei, A. Haas, R.A. Baylis, H. Gao, L. Luo, S.H. Giordano, M.R. Wehner, K.T. Nead, N.J. Leeper, Risk of Cancer after diagnosis of cardiovascular disease, JACC CardioOncol. 5 (2023) 431–440.

[39] L. Mazzolai, G. Teixido-Tura, S. Lanzi, V. Boc, E. Bossone, M. Brodmann, A. Bura-Riviere, J. De Backer, S. Deglise, A. Della Corte, C. Heiss, M. Kaluzna-Oleksy, D. Kurpas, McEniery CM, T. Mirault, A.A. Pasquet, A. Pitcher, Schaubroeck HAI, O. Schlager, P.A. Sirnes, M.G. Sprynger, E. Stabile, F. Steinbach, M. Thielmann, R. R.J. van Kimmenade, M. Venermo, J.F. Rodriguez-Palomares, Group ESCSD, ESC guidelines for the management of peripheral arterial and aortic diseases, Eur. Heart J. 2024 (45) (2024) 3538–3700.