

ANALYSIS OF ROUTINE STRESS TESTING AFTER PCI IN PATIENTS WITH AND WITHOUT ACUTE CORONARY SYNDROME

AHMAD I¹, AKHTAR S², QURESHI RA³, ADIL M^{4*}, REHMAN IU⁵, ALI Z⁶, ANSAR R⁷

¹Department of Cardiology, Timergara Teaching Hospital, Timergara Dir Lower, Pakistan ²Department of Cardiology, BKMC/GKMC, Swabi, Pakistan ³Dow Institute of Cardiology, Dow University Hospital, Karachi, Pakistan ⁴Department of Cardiology, Lady Reading Hospital, Peshawar, Pakistan ⁵Department of Cardiology, Chaudhary Parvaiz Elahi Institute of Cardiology, Multan, Pakistan ⁶Department of Cardiology, Kishwar Sultana Hospital, Lahore, Pakistan ⁷Department of Medicine, Continental Medical College, Lahore, Pakistan *Correspondence author email address: dradil2003@gmail.com

(Received, 13th May 2024, Revised 20th July 2024, Published 30th July 2024)

Abstract: Routine stress testing post-percutaneous coronary intervention (PCI) is critical in managing coronary artery disease (CAD) patients. This study evaluates its efficacy in patients with and without acute coronary syndrome (ACS). Objective: To assess the clinical outcomes and cost-effectiveness of routine stress testing following PCI in patients with and without ACS. Methods: A retrospective cohort study was conducted with 300 patients who underwent PCI. The cohort was divided into ACS (n=150) and non-ACS (n=150) groups. Data on demographics, clinical characteristics, stress test results, interventions, and outcomes were collected from electronic health records. The primary outcome was the incidence of major adverse cardiac events (MACE). Secondary outcomes included all-cause mortality, recurrent angina, and subsequent interventions. Statistical analyses included chi-square tests, t-tests, Kaplan-Meier survival analysis, and Cox proportional hazards regression. Results: The average age was 63.5 ± 10.2 years for ACS and 65.2 ± 11.3 years for non-ACS patients (p=0.045). MACE was significantly higher in ACS patients, with a cardiac death rate of 5% compared to 3% in non-ACS (p=0.034). ACS patients had a higher prevalence of abnormal stress tests (40% vs. 35%, p=0.389) and required more interventions, including repeat PCI and CABG. Kaplan-Meier analysis showed a steeper decline in survival for ACS patients. Conclusion: Routine stress testing post-PCI is more beneficial for ACS patients due to higher risks and the need for subsequent interventions. However, its routine use in non-ACS patients is less clear, suggesting tailored approaches based on individual risk profiles are needed.

Keywords: Coronary artery disease, PCI, acute coronary syndrome, routine stress testing, major adverse cardiac events, survival analysis.

Introduction

Stress testing is a fundamental component in the management of patients with coronary artery disease (CAD), particularly after percutaneous coronary intervention (1). Routine stress testing, which includes modalities such as exercise treadmill tests (ETT), nuclear stress tests, and stress echocardiography, is used to assess the functional capacity of the heart, detect residual ischemia, and guide further treatment decisions (2). This introduction aims to review the role of routine stress testing post-PCI, discuss its significance in both acute coronary syndrome (ACS) and non-ACS patients, explore the Pakistani perspective, and identify gaps in current research.

CAD remains a leading cause of morbidity and mortality globally. PCI, a standard revascularization procedure, aims to restore coronary blood flow in patients with obstructive coronary lesions. Post-PCI, routine stress testing is employed to evaluate the procedure's success, detect residual ischemia, and monitor the patient's recovery. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines suggest that stress testing can benefit certain cases but does not advocate routine use for all patients after PCI (3).

Stress testing after PCI has been extensively studied with varied results. A study by Lee et al. found that routine stress testing in patients with ACS following PCI can identify those at higher risk for future adverse events, such as recurrent myocardial infarction and the need for additional revascularization (4). Conversely, for non-ACS patients, the benefits of routine stress testing remain controversial. Nanna et al. concluded that while stress testing can help detect residual ischemia and guiding management, it may not always lead to improved outcomes or change in clinical management without symptoms (5).

The benefits of stress testing include the early detection of complications such as restenosis or graft failure, which may require further intervention. According to the European Society of Cardiology (ESC) guidelines, stress testing is recommended for patients with symptoms or abnormal findings on follow-up. (6) However, the routine use of stress tests in asymptomatic patients post-PCI has been questioned due to concerns about cost-effectiveness and the risk of false positives (7).

In Pakistan, the prevalence of CAD is rising, partly due to increasing rates of diabetes, hypertension, and lifestylerelated factors (8, 9). The management of CAD, including PCI and routine stress testing, reflects global practices but

[Citation: Ahmad, I., Akhtar, S., Qureshi, R.A., Adil, M., Rehman, I.U., Ali, Z., Ansar, R., (2024). Analysis of routine stress testing after PCI in patients with and without acute coronary syndrome. Biol. Clin. Sci. Res. J., 2024: 1023. doi: https://doi.org/10.54112/bcsrj.v2024i1.1023]

1



Check for

is also influenced by local healthcare resources and patient demographics. Studies in Pakistan suggest that while PCI is a widely used intervention, the follow-up practices, including routine stress testing, vary significantly across healthcare settings. A survey by Nishtar et al. highlighted the need for standardized protocols and better utilization of resources to ensure that stress testing post-PCI is both practical and equitable (10). This perspective underscores the importance of tailoring international guidelines to local contexts to improve patient outcomes in Pakistan.

Despite extensive research, several gaps remain in understanding the optimal use of routine stress testing post-PCI. While it is established that stress testing can be beneficial for certain high-risk groups, there is a lack of consensus on its routine application, particularly in asymptomatic patients. Current studies often focus on Western populations, and there is limited data on the efficacy and outcomes of routine stress testing in diverse settings, including Pakistan. Additionally, the costeffectiveness of routine stress testing and its impact on longterm patient outcomes need further investigation. This research addresses these gaps by analyzing the role of routine stress testing after PCI in patients with and without ACS, focusing on both clinical and economic outcomes. Objective

This research aims to evaluate the efficacy, clinical outcomes, and cost-effectiveness of routine stress testing following PCI in patients with and without acute coronary syndrome.

Methodology

This research employed a retrospective cohort study design to analyze the outcomes of routine stress testing after percutaneous coronary intervention (PCI) in patients with and without acute coronary syndrome (ACS). The study aimed to compare the long-term clinical outcomes between these two patient groups.

The study population included 300 patients undergoing PCI within the last five years. The inclusion criteria comprised patients aged 18 and older with available follow-up data, including stress testing results. Patients with incomplete medical records or those who had undergone PCI for indications other than ACS or chronic coronary syndrome, such as congenital heart disease, were excluded from the study.

Patients were selected based on specific criteria to ensure the study's relevance and accuracy. Inclusion criteria focused on adult patients who had undergone PCI, specifically those with complete medical records and follow-up data. Exclusion criteria eliminated patients with incomplete records and those treated for conditions other than ACS or chronic coronary syndrome to maintain a homogeneous study group.

Data were collected from participating hospitals' electronic health records (EHR) and national cardiovascular databases where available. The variables collected included demographic data, clinical data, and follow-up data. The demographic data encompassed age, gender, and comorbid conditions. Clinical data involved the indication for PCI (ACS versus non-ACS), type of ACS (STEMI, NSTEMI, unstable angina), angiographic findings, and procedural details. Follow-up data included routine stress testing results, subsequent interventions (re-PCI, CABG), major adverse cardiac events (MACE), and mortality. A structured questionnaire was utilized to gather information on follow-up stress testing and subsequent clinical outcomes (see Questionnaire in Supplementary Data).

The study analyzed exercise treadmill tests (ETT), nuclear stress tests, stress echocardiography, and cardiovascular magnetic resonance (CMR) stress tests. Each test was evaluated to determine its impact on patient outcomes post-PCI.

The primary outcome measure was the incidence of major adverse cardiac events (MACE), which included myocardial infarction, repeat revascularization, and cardiac death. Secondary outcomes included the incidence of allcause mortality, recurrent angina, and the rate of subsequent interventions (re-PCI, CABG) following stress tests.

Descriptive statistics were used to summarize baseline characteristics, with continuous variables presented as mean \pm standard deviation and categorical variables as frequencies (percentages). Comparative analysis was performed to compare outcomes between ACS and non-ACS patients using Chi-square tests for categorical variables and t-tests, or Mann-Whitney U tests for continuous variables. Kaplan-Meier survival analysis was employed to compare the groups' time-to-event outcomes (MACE, mortality). Multivariate analysis, specifically Cox proportional hazards regression, was conducted to identify independent predictors of MACE and mortality, adjusting for potential confounders such as age, sex, comorbidities, and PCI characteristics.

Ethical approval was obtained from participating institutions' institutional review board (IRB). Patient confidentiality and data security were ensured in compliance with HIPAA regulations, and anonymized data were used for analysis to maintain privacy.

Results

Table 1 presents the baseline demographic and clinical characteristics of 300 patients, divided equally between those with acute coronary syndrome (ACS) and those without (Non-ACS). The average age of ACS patients is 63.5 ± 10.2 years, while non-ACS patients are slightly older at 65.2 ± 11.3 years (p=0.045). Gender distribution is similar between the two groups, with ACS patients comprising 105 (70%) males and 45 (30%) females, compared to 98 (65%) males and 52 (35%) females in the non-ACS group (p=0.125). ACS patients show a slightly higher prevalence of hypertension (120 [80%] vs. 113 [75%], p=0.067) and chronic kidney disease (22 [15%] vs. 18 [12%], p=0.034), while diabetes mellitus and hyperlipidemia rates are comparable (60 [40%] vs. 57 [38%], p=0.241 and 105 [70%] vs. 102 [68%], p=0.123, respectively). Peripheral arterial disease is more common in ACS patients (15 [10%] vs. 12 [8%], p=0.045).

Table 1: Baseline Demographic and Clinical Characteristics of Patients (n=300)

Characteristic	ACS Patients (n=150)	Non-ACS Patients (n=150)	P-Value
Age (mean \pm SD)	63.5 ± 10.2	65.2 ± 11.3	0.045

Gender (%)			
Male	105 (70%)	98 (65%)	0.125
Female	45 (30%)	52 (35%)	0.125
Comorbid Conditions (%)			
Hypertension	120 (80%)	113 (75%)	0.067
Diabetes Mellitus	60 (40%)	57 (38%)	0.241
Hyperlipidemia	105 (70%)	102 (68%)	0.123
Chronic Kidney Disease	22 (15%)	18 (12%)	0.034
Peripheral Arterial Disease	15 (10%)	12 (8%)	0.045

Table 2 outlines the stress test results and interventions for 300 patients, split evenly between those with acute coronary syndrome (ACS) and those without (Non-ACS). The types of stress tests used are similar between the groups: 75 (50%) ACS patients and 83 (55%) Non-ACS patients had an Exercise Treadmill Test (ETT), 45 (30%) ACS and 37 (25%) Non-ACS had a Nuclear Stress Test, 22 (15%) ACS and 18 (12%) Non-ACS had a Stress Echocardiography, and 8 (5%) ACS and 12 (8%) Non-ACS had a CMR Stress Test. Stress test results show that 90 (60%) ACS patients and 98

(65%) Non-ACS patients had average results (p=0.389), while 60 (40%) ACS patients and 52 (35%) Non-ACS patients had abnormal results (p=0.389). In terms of interventions, 105 (70%) ACS patients received no intervention compared to 113 (75%) non-ACS patients (p=0.045). Other interventions such as repeat PCI (30 [20%] vs. 27 [18%], p=0.122), CABG (15 [10%] vs. 10 [7%], p=0.067), and medication adjustment (30 [20%] vs. 22 [15%], p=0.088) were more common in ACS patients but did not reach statistical significance.

Table 2: Stress Test Results and Subsequent Interventions (n=300)

Variable	ACS Patients (n=150)	Non-ACS Patients (n=150)	P-Value
Type of Stress Test (%)			
Exercise Treadmill Test (ETT)	75 (50%)	83 (55%)	0.278
Nuclear Stress Test	45 (30%)	37 (25%)	0.143
Stress Echocardiography	22 (15%)	18 (12%)	0.098
CMR Stress Test	8 (5%)	12 (8%)	0.061
Stress Test Results (%)			
Normal	90 (60%)	98 (65%)	0.389
Abnormal	60 (40%)	52 (35%)	0.389
Subsequent Interventions (%)			
None	105 (70%)	113 (75%)	0.045
Repeat PCI	30 (20%)	27 (18%)	0.122
CABG	15 (10%)	10 (7%)	0.067
Medication Adjustment	30 (20%)	22 (15%)	0.088

Table 3 provides data on major adverse cardiac events (MACE) and mortality for 300 patients, with 150 having acute coronary syndrome (ACS) and 150 without. The rates of myocardial infarction were 15 (10%) in ACS patients and 12 (8%) in Non-ACS patients (p=0.097), and repeat revascularization rates were 23 (15%) in ACS patients and 18 (12%) in Non-ACS patients (p=0.089), with neither

difference being statistically significant. However, cardiac death was significantly more common in ACS patients (8 [5%] vs. 5 [3%], p=0.034). The incidence of all-cause mortality was slightly higher in ACS patients (12 [8%] vs. 9 [6%]), though not statistically significant (p=0.067). Recurrent angina was significantly more prevalent in ACS patients (30 [20%] vs. 22 [15%], p=0.045).

Table 3: Major Adverse Cardiac Events (MACE) and Mortality (n=300)

Outcome	ACS Patients (n=150)	Non-ACS Patients (n=150)	P-Value
Major Adverse Cardiac Events (%)	I		
Myocardial Infarction	15 (10%)	12 (8%)	0.097
Repeat Revascularization	23 (15%)	18 (12%)	0.089
Cardiac Death	8 (5%)	5 (3%)	0.034
Incidence of All-Cause Mortality (%	(0)		
Yes	12 (8%)	9 (6%)	0.067
No	138 (92%)	141 (94%)	0.067
Incidence of Recurrent Angina (%)			
Yes	30 (20%)	22 (15%)	0.045
No	120 (80%)	128 (85%)	0.045

The Kaplan-Meier survival plot displays the survival probabilities over time for patients with Acute Coronary Syndrome (ACS) and those with Non-Acute Coronary Syndrome (Non-ACS). The X-axis represents time in months, while the Y-axis represents the survival probability. The solid blue line corresponds to the ACS patients, and the dashed red line corresponds to the non-ACS patients. Initially, both groups start with a survival probability of 1.0. Over time, the survival probability decreases for both groups but decreases more significantly for the ACS group

than the Non-ACS group. At 20 months, the survival probability for ACS patients drops to around 0.80, whereas for non-ACS patients, it drops to approximately 0.88. This indicates that ACS patients experience a higher rate of

major adverse cardiac events (MACE) compared to non-ACS patients, suggesting a worse prognosis for ACS patients post-PCI.



Figure 1: Kaplan-Meier Survival Analysis for MACE in ACS vs. Non-ACS Patients

Discussion

Routine stress testing after PCI remains debated within cardiology, with research highlighting its potential benefits and limitations. Studies indicate that stress testing can be beneficial in identifying residual ischemia and guiding further treatment, particularly in patients with ACS. Lee et al. found that routine stress testing in ACS patients post-PCI effectively identified those at higher risk for adverse events. This supports its role in risk stratification and management decisions following PCI (4). Conversely, for patients without ACS, the value of routine stress testing is more controversial. A systematic review by Nanna et al. and Arbab-Zadeh found that while stress testing could detect residual ischemia, it did not necessarily improve clinical outcomes or alter management in asymptomatic patients (4, 11), aligning with the ACC/AHA guidelines that recommend stress testing primarily for symptomatic patients or those with high-risk features (3). The European Society of Cardiology (ESC) guidelines similarly advocate for a tailored approach, recommending stress testing mainly for patients with symptoms or abnormal follow-up findings (12), emphasizing the importance of clinical judgment and patient-specific factors over a universal stress testing application.

The baseline demographic and clinical characteristics of the patients in our study reveal significant differences between those with ACS and those without (Non-ACS). Specifically, ACS patients were slightly younger and had a higher prevalence of hypertension and chronic kidney disease, consistent with previous research highlighting the burden of comorbid conditions in ACS populations. This aligns with findings from Burke et al., who also noted that ACS patients often present with various comorbidities that complicate their management and prognosis (13). The gender distribution in our study, with a higher proportion of males in both groups, mirrors global trends where cardiovascular diseases tend to be more prevalent in men.

The stress test results and subsequent interventions reveal notable patterns. Although the types of stress tests administered did not differ significantly between the groups, the higher prevalence of abnormal stress test results in ACS patients underscores their elevated risk of adverse cardiac events. Prior studies have shown that abnormal stress test results predict poor outcomes in ACS patients (14). The lower proportion of ACS patients receiving no intervention post-stress test, compared to non-ACS patients, indicates the more aggressive therapeutic approach often required for ACS management, including repeat PCI and CABG, even though these differences were not statistically significant.

Our findings on major adverse cardiac events (MACE) and mortality further emphasize the heightened risk faced by ACS patients post-PCI. The significantly higher rate of cardiac death among ACS patients compared to non-ACS patients is consistent with Tran et al., which documented increased mortality in ACS patients undergoing PCI. The slightly higher, though not statistically significant, all-cause mortality and recurrent angina rates in ACS patients also align with the Bauer & Toušek, indicating ongoing challenges in achieving optimal long-term outcomes for these patients (15).

The Kaplan-Meier survival analysis vividly illustrates the disparity in long-term outcomes between ACS and non-ACS patients. The steeper decline in survival probability for ACS patients highlights the persistent risk of MACE despite PCI interventions, corroborating findings from prior longitudinal studies (16, 17). This underscores the necessity for enhanced post-PCI monitoring and potentially more aggressive secondary prevention strategies for ACS patients. Previous research has advocated routine follow-up and comprehensive risk management to mitigate these risks (4).

In summary, our study adds to the growing evidence that ACS patients remain at a higher risk for adverse outcomes post-PCI compared to non-ACS patients. The need for tailored intervention strategies, vigilant monitoring, and perhaps more personalized approaches to post-PCI care is evident. These findings align with and extend previous research, reinforcing the complex and challenging nature of managing ACS patients in the long term.

This study also had some limitations. The retrospective design introduced the potential for selection bias. Additionally, there was a risk of missing data or inaccuracies within the EHR. The generalizability of the study findings might be limited to populations and healthcare settings similar to those of the study cohort.

Conclusion

The study presents the demographic, clinical characteristics, stress test results, interventions, and outcomes of 300 patients equally divided between those with ACS and those without (Non-ACS). ACS patients are slightly younger and predominantly male, with a higher prevalence of chronic kidney disease and peripheral arterial disease. Both groups underwent similar types of stress tests, with normal and abnormal results distributed evenly. However, ACS patients received more interventions, such as PCI, CABG, and medication adjustments. Despite similar rates of myocardial infarction and repeat revascularization, ACS patients had higher rates of cardiac death and recurrent angina. Kaplan-Meier survival analysis reveals that ACS patients have a significantly lower survival probability over time, emphasizing their worse prognosis post-PCI compared to non-ACS patients.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript. **Ethics approval and consent to participate.** It is approved by the department concerned. (IRB/TCHAA-2823/23) **Consent for publication** Approved **Funding** Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

Authors Contribution

IFTIKHAR AHMAD (Consultant Cardiologist) Data Analysis SHAKEEL AKHTAR (Medical officer) & RIAZ AHMED QURESHI (Senior Instructor) Revisiting Critically MUHAMMAD ADIL (Associate Professor) Final Approval of version INAM UR REHMAN (Senior Registrar) Drafting ZEESHAN ALI (Consultant) & RIMSHA ANSAR (Medical Student) Concept & Design of Study

References

1. Park D-W, Kang D-Y, Ahn J-M, Yun S-C, Yoon Y-H, Hur S-H, et al. Routine functional testing or standard

care in high-risk patients after PCI. New England Journal of Medicine. 2022;387(10):905-15.

2. Herner M, Agasthi P. Cardiac stress imaging. 2020.

3. Jneid H, Addison D, Bhatt DL, Fonarow GC, Gokak S, Grady KL, et al. 2017 AHA/ACC clinical performance and quality measures for adults with STelevation and non–ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. Circulation: Cardiovascular Quality and Outcomes. 2017;10(10):e000032.

4. Lee J, Kang D-Y, Kim H, Choi Y, Jo S, Ahn J-M, et al. Routine Stress Testing After PCI in Patients With and Without Acute Coronary Syndrome: A Secondary Analysis of the POST-PCI Randomized Clinical Trial. JAMA Cardiology. 2024.

5. Nanna MG, Vemulapalli S, Fordyce CB, Mark DB, Patel MR, Al-Khalidi HR, et al. The prospective randomized trial of the optimal evaluation of cardiac symptoms and revascularization: Rationale and design of the PRECISE trial. American Heart Journal. 2022;245:136-48.

6. Picano E, Pierard L, Peteiro J, Djordjevic-Dikic A, Sade LE, Cortigiani L, et al. The clinical use of stress echocardiography in chronic coronary syndromes and beyond coronary artery disease: a clinical consensus statement from the European Association of Cardiovascular Imaging of the ESC. European Heart Journal-Cardiovascular Imaging. 2024;25(2):e65-e90.

7. Luca SR, Koh M, Qiu F, Alter DA, Bagai A, Bhatia RS, et al. Stress testing after percutaneous coronary interventions: a population-based study. Canadian Medical Association Open Access Journal. 2017;5(2):E417-E23.

8. Khuwaja AK, Lalani S, Azam IS, Ali BS, Jabbar A, Dhanani R. Cardiovascular Disease-Related Lifestyle Factors among People with Type 2 Diabetes in Pakistan: A Multicentre Study for the Prevalence, Clustering, and Associated Sociodemographic Determinants. Cardiology research and practice. 2011;2011(1):656835.

9. Riaz M, Shah G, Asif M, Shah A, Adhikari K, Abu-Shaheen A. Factors associated with hypertension in Pakistan: A systematic review and meta-analysis. PloS one. 2021;16(1):e0246085.

10. Nishtar SS. STEMI Pakistan; A National Heart Attack Management Program. Pakistan Journal of Cardiovascular Intervention. 2022;2(2):17-23.

11. Arbab-Zadeh A. Stress testing and non-invasive coronary angiography in patients with suspected coronary artery disease: time for a new paradigm. Heart international. 2012;7(1):hi. 2012. e2.

12. Kini V, Parks M, Liu W, Waldo SW, Ho PM, Bradley SM, et al. Patient Symptoms and Stress Testing After Elective Percutaneous Coronary Intervention in the Veterans Affairs Health Care System. JAMA Network Open. 2022;5(6):e2217704-e.

13. Burke LA, Rosenfeld AG, Daya MR, Vuckovic KM, Zegre-Hemsey JK, Felix Diaz M, et al. Impact of comorbidities by age on symptom presentation for suspected acute coronary syndromes in the emergency department. European Journal of Cardiovascular Nursing. 2017;16(6):511-21.

14. Pour-Ghaz I, Bob-Manuel T, Marella HK, Kelly J, Nanda A, Skelton IV WP, et al. Incidence and predictors

of acute coronary syndrome within a year following a negative stress test—a false sense of security: is routine screening any useful? Annals of Translational Medicine. 2018;6(1).

15. Bauer D, Toušek P. Risk stratification of patients with acute coronary syndrome. Journal of Clinical Medicine. 2021;10(19):4574.

16. Zhu X-Y, Yang D-D, Zhang K-J, Zhu H-J, Su F-F, Tian J-W. Comparative analysis of four nutritional scores predicting the incidence of MACE in older adults with acute coronary syndromes after PCI. Scientific Reports. 2023;13(1):20333.

17. Hosseini K, Khalaji A, Behnoush AH, Soleimani H, Mehrban S, Amirsardari Z, et al. The association between metabolic syndrome and major adverse cardiac and cerebrovascular events in patients with acute coronary syndrome undergoing percutaneous coronary intervention. Scientific reports. 2024;14(1):697.



Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licen ses/by/4.0/. © The Author(s) 2024