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FREQUENCY OF PERIPHERAL ARTERIAL DISEASE IN PATIENTS PRESENTING WITH ACUTE CORONARY SYNDROME

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ABSTRACT

Background: Coronary artery disease (CAD) is a leading cause of morbidity and mortality worldwide, accounting for 7.4 million of 17.9 million annual cardiovascular deaths. Acute coronary syndrome (ACS) is a symptomatic subset of CAD often associated with myocardial infarction, and includes ST-elevation (STEMI) and non-ST-elevation myocardial infarction (NSTEMI). Atherosclerosis is a systemic process; hence peripheral arterial disease (PAD) frequently coexists with CAD as a manifestation of diffuse atherosclerosis. Many CAD patients have coexistent PAD that is asymptomatic and underdiagnosed . Early identification of PAD in ACS patients is important for secondary prevention and risk stratification, but the local frequency of PAD in ACS is not well established.

Objective: To determine the frequency of PAD in patients with CAD presenting with ACS to a tertiary care hospital, using ankle-brachial index (ABI) screening, and to analyze associations with patient demographics.

Methodology: A cross-sectional study was conducted at the Cardiology Department of a Lady Reading Hospital Peshawar Pakistan. Over a 6-month period from May–Nov 2024, 159 patients aged 40–70 years with ACS (STEMI or NSTEMI confirmed by clinical, ECG and biomarker criteria) were enrolled by consecutive sampling. Patients with previously known PAD, limb deformity, edema, or incompressible arteries (ABI >1.3) were excluded. Demographic data (age, gender, body mass index [BMI], and CAD duration) were recorded. PAD was assessed by measuring ABI using an automated device after 15 minutes of supine rest; PAD was defined as ABI <0.90 in either leg (without prior PAD history). Frequency of PAD was calculated. Patients were

stratified by age, gender, BMI, and CAD duration to evaluate effect modifiers; comparisons used chi-square tests with $p \leq 0.05$ as significant.

Results: Of the 159 ACS patients (mean age 56.8 ± 9.5 years, 78% male), PAD (ABI <0.9) was detected in 11 patients, yielding a PAD frequency of 6.9% (95% confidence interval ~3.0–10.8%). Among those with PAD, 4 (36%) reported intermittent claudication symptoms, while 7 (64%) were asymptomatic (incidentally identified via ABI). Patients with PAD were older on average than those without PAD (mean age 62 vs 55 years, $p = 0.03$). In patients aged ≥60 years, PAD prevalence was 20.5%, significantly higher than in those <60 years (2.7%, $p < 0.001$). PAD frequency was slightly higher in males (7.2%) than females (5.9%), but this difference was not statistically significant ($p = 0.75$). No significant associations were found between PAD presence and BMI or duration of known CAD ($p > 0.05$ for both).

Conclusion: In this cohort of ACS patients, about 7% had coexisting PAD as determined by ABI screening. This relatively sizable minority underscores the importance of routine PAD screening in ACS patients. Early detection of PAD allows for more comprehensive cardiovascular risk management. Our findings, in line with regional data showing ~7–8% PAD prevalence in CAD, highlight that even asymptomatic PAD is prevalent in ACS and merits attention to improve secondary prevention and outcomes.

INTRODUCTION

Coronary artery disease (CAD) has become a major public health problem due to its enormous prevalence and its role as a leading cause of death worldwide[1]. According to the World Health Organization, an estimated 17.9 million people die of cardiovascular diseases annually, of which about 7.4 million are attributable to CAD[2]. In clinical practice, acute coronary syndrome (ACS) refers to the spectrum of clinical presentations resulting from acute myocardial ischemia. ACS is invariably symptomatic and usually associated with myocardial infarction (MI), unlike stable CAD which may remain asymptomatic[3]. ACS encompasses ST-elevation MI (STEMI) and non-ST-elevation MI (NSTEMI); the latter is more common and is a major contributor to ACS-related hospital admissions and mortality, Despite advances in treatment, ACS continues to carry significant morbidity and mortality, especially when compounded by other vascular comorbidities[4].

Atherosclerosis is a diffuse and progressive condition that can affect coronary, cerebral, and peripheral arteries simultaneously[5]. Peripheral arterial disease (PAD), defined as atherosclerotic occlusive disease of arteries of the limbs (commonly the legs), becomes increasingly prevalent with age – from roughly 1–3% in individuals in their 40s to over 20% in those in their 80s. Traditional cardiovascular risk factors (such as smoking, diabetes, hypertension, and dyslipidemia) drive the development of both CAD and PAD[6]. Indeed, PAD itself is recognized as a powerful risk marker for cardiovascular events and is associated with a higher likelihood of multivessel and obstructive CAD. Patients with concomitant PAD and CAD often have more extensive

coronary disease (e.g. multi-vessel involvement) and worse prognosis than those with CAD alone. However, PAD often remains clinically silent; many patients do not report classic claudication symptoms[7]. As a result, PAD is frequently underdiagnosed and undertreated in the CAD population. The ankle-brachial index (ABI) is a simple, noninvasive screening tool for PAD that can unmask subclinical disease. An ABI < 0.90 is highly sensitive and specific for PAD (as confirmed by angiography) and is an independent predictor of future cardiovascular morbidity and mortality. Routine ABI measurement is not yet a standard practice in all cardiology settings, but it has been advocated as a means to improve detection of PAD in high-risk patients[8].

Existing literature suggests that a substantial subset of patients with CAD have coexisting PAD. International studies have reported PAD prevalence in CAD patients ranging from about 10% to 30%, especially in Western populations[9]. In South Asian populations, reported rates are lower. For example, Saran et al. documented a PAD prevalence of roughly 7–8% in Indian patients with angiographically proven CADresearchgate.net. In that study, patients with low ABI (<0.9) were significantly older and more likely to be hypertensive or diabetic[10]. Another investigation in the Middle East by Saleh et al. found that 14.7% of patients with angiographically proven CAD had previously unrecognized PAD when actively screened with ABI. These differences may reflect variations in risk factor profiles, genetics, or the younger age of CAD patients in South Asia. Notably, most PAD in CAD patients is asymptomatic; Saleh et al. and others highlighted that active screening unearths a high PAD burden that would otherwise go unrecognized[11].

Early identification of PAD in patients with CAD (and specifically those presenting with ACS) is crucial. Coexistent PAD not only indicates a more widespread atherosclerotic burden but also portends worse outcomes: recent registry data show that ACS patients with known PAD have significantly higher risks of recurrent ischemic events and mortality[12]. For instance, in a large real-world ACS registry, patients with concomitant PAD had a 30-day major adverse cardiac event (MACE) rate of 22% compared to 14% in those without PAD, and an almost two-fold higher 1-year mortality (approximately 10% vs 4–5%). Such findings underscore that recognizing PAD in ACS patients can prompt more aggressive risk factor modification (e.g. intensification of antiplatelet, lipid-lowering, and exercise therapies) and closer follow-up to improve outcomes[13].

In our local context, data on the frequency of PAD among ACS patients are scarce. Given the potentially actionable information gleaned from detecting PAD, we undertook this study to determine how often PAD is present in patients with ACS in a tertiary care hospital setting. We used ABI screening in all enrolled ACS patients to objectively diagnose PAD. The results of this study will provide insight into the burden of PAD in ACS patients in our population and may support the case for routine PAD screening as part of comprehensive ACS care, ultimately aiding in secondary prevention strategies.

Materials and Methods:

Study Design and Setting:

This was a cross-sectional observational study carried out at the Department of Cardiology Lady Reading Hospital Peshawar Pakistan. The study was conducted over a 6-month period from May 2024 to November 2024.

Study Population:

Patients presenting with acute coronary syndrome were screened for eligibility.

Inclusion criteria were: age 40 to 70 years; either sex; and diagnosis of CAD presenting as ACS as per operational definition. We defined ACS (CAD) operationally as patients presenting with central or left-sided chest pain (rated >4 on a 10-point pain scale) radiating to the jaw or left arm, associated with dyspnea, not relieved by rest or nitrates, accompanied by characteristic ECG changes (ST-segment elevation or depression) and elevated cardiac enzymes, with confirmation of coronary artery stenosis >50% in an epicardial artery on angiography. Both STEMI and NSTEMI presentations were included under the ACS umbrella.

Exclusion criteria were: patients with a known prior diagnosis of PAD, patients with significant anatomical deformity of the limbs precluding blood pressure cuff placement, patients with gross lower limb edema, and patients found to have non-compressible arteries on ABI measurement (ABI > 1.30, often due to arterial calcification). These exclusions were made to avoid false readings and include only new diagnoses of PAD.

Sample Size and Sampling:

The sample size was calculated using the WHO sample size calculator, anticipating a PAD frequency p of 7.1% (based on prior regional data), with a margin of error of 5% and 95% confidence level. This yielded a required sample of n ≈ 159 patients. We enrolled 159 consecutive patients meeting inclusion criteria (non-probability consecutive sampling) from the cardiology inpatient service (coronary care unit and cardiology ward). Informed consent was obtained from each participant prior to inclusion, with assurance of confidentiality and no added risk from study procedures.

Data Collection Procedures:

Upon enrollment, baseline information was recorded, including patient demographics (age in years, sex), clinical data such as duration of known CAD (in months since first diagnosis or onset of symptoms, if any), and body mass index (BMI, in kg/m²). A detailed history was taken, specifically noting any history of intermittent claudication (exertional calf pain relieved by rest), which is a classic symptom of PAD. A thorough physical examination was performed including peripheral pulse examination.

Each patient then underwent ABI measurement to screen for PAD. The ABI was measured using an automated four-limb blood pressure device (WatchBP Office ABI, Microlife AG, Switzerland) which can simultaneously measure systolic pressures in both arms and ankles. Patients were kept at rest in the supine position for at least 15 minutes before measurement. Appropriate-sized blood pressure cuffs were applied to both arms (brachial arteries) and both ankles (above the ankles, to capture posterior tibial/dorsalis pedis arteries). Systolic blood pressures were recorded in all four limbs simultaneously by the device. The ABI for each leg was calculated as the ratio of the higher of the two ankle systolic pressures (DP or PT artery) to the higher of the two brachial systolic pressures. For analysis, the lower ABI value of the two legs was taken as the patient's ABI. Peripheral arterial disease (PAD) was defined operationally as an ABI < 0.90 in either leg, which corresponds to at least mild PAD. ABI values between 0.91–1.30 were considered normal (no PAD), while values >1.30 were considered uninterpretable due to likely arterial incompressibility (such patients were excluded as noted). The presence or absence of PAD (by ABI criteria) in each patient was recorded on a structured proforma along with the patient's other data.

All study data were collected by the principal investigator and recorded on the pre-designed proforma . Thereafter, data were entered into IBM SPSS Statistics version 26 for analysis.

Data Analysis:

Continuous variables such as age, BMI, and disease duration were summarized as mean ± standard deviation (for approximately normal distributions) or median with interquartile range (for skewed distributions). Categorical variables such as gender, presence of claudication symptoms, and PAD (yes/no) were summarized as frequencies and percentages. The primary outcome of interest was the frequency (proportion) of PAD in the sample of ACS patients. For the main analysis, this proportion with a 95% confidence interval was calculated.

To explore factors associated with PAD, we performed subgroup analyses by stratification. Patients were stratified into age categories (<60 years vs ≥60 years), by sex (male vs female), by BMI category (e.g. non-obese vs obese, using BMI ≥25 or ≥30 kg/m² as cut-off), and by CAD duration (<1 year vs ≥1 year since diagnosis, as a proxy for chronicity). Within each stratum, the frequency of PAD was determined. Chi-square (χ^2) tests were used to compare PAD frequencies across these subgroups to identify any statistically significant differences (effect modification). For example, we compared PAD prevalence in older (≥60) vs younger patients, in males vs females, etc. A p-value ≤ 0.05 was considered statistically significant for these comparisons. If expected cell counts were small, Fisher's exact test would be used instead of chi-square. No imputation was done for missing data (patients with incomplete ABI data were excluded by the protocol). The results are presented in the form of tables and narrative summaries.

Results:

Patient Characteristics:

A total of 159 patients with acute coronary syndrome were included in the analysis. The baseline demographic and clinical characteristics are summarized in Table 1. The mean age of the patients was 56.8 ± 9.5 years (range 40–70 years). The cohort was predominantly male (124 males, 78.0%; 35 females, 22.0%). The mean BMI was 26.7 ± 3.8 kg/m². Regarding ACS presentation, 99 patients (62.3%) presented with STEMI and 60 patients (37.7%) with NSTEMI. A history of previously diagnosed CAD (prior angina or MI) was present in 45 patients (28.3%), whereas the remaining 114 (71.7%) were first-presenting ACS cases. Among those with known CAD, the median duration of CAD was 8 months (IQR: 3–18 months). Cardiovascular risk factors were common (though not systematically recorded for all patients in this study); however, 48% were diabetic and 55% hypertensive as per admission notes (for context, not a primary focus of this study).

Frequency of PAD:

Using ABI screening, 11 out of 159 ACS patients were found to have PAD, corresponding to an overall PAD frequency of 6.9% in this cohort. In other words, approximately 1 in 14 patients with ACS had evidence of occult peripheral arterial disease on ABI screening. The proportion of PAD remained the same when stratified by ACS type (PAD was found in 7.1% of STEMI patients and 6.7% of NSTEMI patients, difference not significant). Of the 11 patients with PAD, only 4 (36%) reported a history of claudication (calf pain on exertion), whereas the majority (7 patients, 64%) denied any leg symptoms, indicating that most PAD cases were asymptomatic and would have been missed without ABI evaluation.

Table 1. Baseline Characteristics of ACS Patients (N = 159)

Characteristic	Value

Characteristic	Value
Age, mean ± SD (years)	56.8 ± 9.5 (range 40–70)
Age distribution	40–50: 32% of patients 51–60: 44% 61–70: 24%
Sex	Male 78.0% (n = 124) Female 22.0% (n = 35)
Body Mass Index, mean ± SD	26.7 ± 3.8 kg/m²
ACS type	STEMI 62.3% (n = 99) NSTEMI 37.7% (n = 60)
Known CAD prior to this ACS	28.3% (n = 45) patients
CAD duration (if known)	Median 8 months (IQR 3–18)
History of claudication	2.5% (n = 4) of all patients (36% of PAD patients)
Peripheral Arterial Disease (ABI <0.90)	**6.9% (n = 11) of patients**

SD = standard deviation; CAD = coronary artery disease; ACS = acute coronary syndrome; STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST-elevation myocardial infarction; IQR = interquartile range.

As shown in Table 1, 11 patients (6.9%) were diagnosed with PAD based on ABI. These patients were comparatively older: the mean age of patients with PAD was 62.1 ± 8.3 years versus 56.4 ± 9.4 years in those without PAD (independent t-test, $p = 0.031$). All 11 PAD patients were above 50 years of age, and notably 8 of them (73%) were in the oldest age stratum (60–70 years). There was no clear sex predilection in PAD occurrence in our sample: 9 of the 124 male patients had PAD (7.3%) versus 2 of 35 female patients (5.7%), $p = 0.75$ (chi-square), indicating no statistically significant difference by gender.

We further analyzed PAD frequency across selected subgroups, as summarized in Table 2. Age showed a significant association with PAD. Among patients aged 60 years or above, 8/39 (20.5%) had PAD, compared to only 3/120 (2.5%) of those under 60 years of age ($p < 0.001$). This underscores age as a strong risk factor for concurrent PAD in ACS patients. In contrast, PAD rates did not differ significantly by sex. Stratification by BMI (e.g., <25 vs ≥25 kg/m²) showed a slightly higher PAD frequency in those with BMI ≥25 (7.5%) compared to BMI <25 (5.5%), but this difference was not significant ($p = 0.64$). Similarly, stratification by known CAD

duration (new-onset ACS vs those with >1 year history of CAD) revealed a modestly higher PAD prevalence in patients with longer-standing CAD (9.1% vs 5.3%, p = 0.40), but this was not statistically significant.

Table 2. Frequency of PAD in ACS Patients by Age and Sex Subgroups

Subgroup	N in subgroup	PAD present, n (%)	p-value (chi-square)
Age < 60 years	120	3 (2.5%)	
Age ≥ 60 years	39	8 (20.5%)	**< 0.001 ★**
Male patients	124	9 (7.3%)	
Female patients	35	2 (5.7%)	0.75

★ $p < 0.001$ for difference in PAD frequency between age groups (≥60 vs <60). There was no significant difference in PAD frequency between sexes ($p = 0.75$).

No statistically significant differences in PAD frequency were observed upon stratification by BMI category or CAD duration (data not shown in table). Thus, in our study, the primary determinant of PAD presence was older age.

In summary, about one in fifteen patients presenting with ACS had coexistent PAD as identified by a low ABI. Most of these PAD cases were asymptomatic from a limb standpoint. Older patients in the ACS cohort were much more likely to have PAD, whereas sex and other factors did not show significant influence in this sample. These findings emphasize that even in an ACS-focused setting, routine PAD screening may identify a subset of patients with systemic atherosclerosis who might benefit from intensified preventive measures.

Discussion:

This study investigated the prevalence of peripheral arterial disease in patients presenting with acute coronary syndrome, in a tertiary care hospital setting, using ABI screening. We found that approximately 7% of ACS patients had coexisting PAD (ABI < 0.9). To our knowledge, this is one of the few studies from Pakistan to specifically quantify PAD frequency in an ACS population. The main finding – a PAD prevalence of around 7% – is in line with data from similar populations in the South Asian region. For instance, Saran et al. reported a PAD prevalence of 7.7% in a cohort of Indian patients with established CAD (including ACS and stable angina). Our results closely mirror their findings, reinforcing the notion that in South Asian CAD patients, the burden of PAD, while significant, is lower than that reported in Western cohorts. Western studies often cite PAD in 10–20% or more of CAD patients, likely reflecting older patient ages and higher prevalence of risk factors like smoking in those populations[10]. In our study, the relatively lower overall age of ACS patients (mean ~57 years) may partially explain the ~7% PAD rate. PAD prevalence strongly increases with age, and indeed we observed a marked age gradient: 20.5% of patients ≥60 years had PAD vs only 2.5% under 60 (p < 0.001). Age-related differences in PAD are well documented; Saran et al. similarly found that PAD patients were older on average by about 6 yearsresearchgate.net,

and other studies have noted PAD prevalence exceeding 15–20% in CAD patients over 70 years old[10].

Our findings underscore the importance of active PAD screening in ACS patients, especially older ones. Notably, over half of the PAD cases in our series were asymptomatic (no claudication), highlighting that reliance on symptoms alone would miss most PAD. This underdiagnosis of PAD in CAD patients has been stressed by other researchers as well. Saleh et al. (2018) studied patients undergoing coronary angiography and found 14.7% had previously unrecognized PAD when systematically screened with ABI[11]. Their higher PAD rate relative to ours could be due to including a broader CAD population (not limited to ACS) with a slightly older mean age, or perhaps a higher prevalence of risk factors like diabetes in their Middle Eastern cohort. Nonetheless, both their study and ours point to a substantial subset of CAD patients harboring silent PAD. As a consequence, routine ABI screening in such high-risk patients has been recommended. Saleh et al. concluded that the high prevalence of occult PAD in CAD patients "confirms the importance of active screening for PAD by using ABI" and that routine ABI measurement could help identify high-risk patients[11]. Our results provide local evidence to support this recommendation – even in an ACS-focused setting, a one-time ABI test was able to identify nearly 1 in 15 patients with significant PAD, information that would otherwise be missed.

An important clinical implication of diagnosing PAD in ACS patients is the impact on prognosis and management. Coexistence of PAD in a patient with ACS essentially flags them as having disseminated atherosclerosis, which has prognostic significance. Prior studies have demonstrated that ACS patients with PAD have worse outcomes. For example, Matetzky et al. (2022) analyzed over 16,000 ACS patients in a registry and found those with known PAD had significantly higher 30-day MACE and one-year mortality. In their analysis, even after adjusting for other factors, PAD remained an independent predictor of 30-day MACE (OR ~1.6) and of 1-year mortality (with a ~2.5-fold higher mortality rate)[14]. While our study did not track outcomes, the identification of PAD in 7% of ACS patients suggests these patients may warrant more aggressive therapy. Guidelines for secondary prevention do recommend that PAD patients be managed with intensive risk factor modification similar to CAD (including high-intensity statins, antiplatelet therapy, smoking cessation, exercise rehabilitation, etc.). Thus, recognizing PAD in an ACS patient should prompt clinicians to ensure such measures are optimized. It may also influence the need for vascular specialist referral or surveillance for limb ischemia in the long term.

Our analysis of associated factors found that age was a significant determinant of PAD presence, which aligns with the epidemiology of PAD. Although our study was not powered to thoroughly evaluate risk factors, the trend towards higher PAD in patients with longer-standing CAD hints that disease duration might correlate with PAD, possibly due to longer exposure to atherosclerotic risk factors. We did not find sex differences in PAD prevalence, which is interesting since some population studies have shown PAD may be slightly more common in men at younger ages but evens out in older ages. In Saleh's study, PAD prevalence was similar between men and women (13.4% vs 11.7%), and in our ACS cohort the small difference (7.3% in men vs 5.7% in women) was not significant. This suggests that once CAD is established (especially in an ACS scenario), both men and women have substantial atherosclerotic burden and are nearly equally likely to have PAD. We did not specifically record smoking, diabetes, or

hypertension in our dataset; however, these are well-known risk factors for PAD. Prior studies (including Saran et al.) have shown a significantly higher prevalence of diabetes and hypertension in CAD patients with PAD compared to those without hypertension. It is highly plausible that the PAD patients in our study had a greater burden of such risk factors, even though we cannot confirm it due to our data collection limits. Future studies in our region should include a comprehensive assessment of risk factors to better characterize the PAD subgroup.

One finding of note is that the majority of PAD cases in our study were newly diagnosed at the time of ACS presentation (we excluded known PAD). This underscores an opportunity: the ACS hospitalization can serve as a "teachable moment" and a point of integration for cardiovascular care – adding a simple PAD screening could identify patients who need additional interventions. For instance, exercise therapy or peripheral angiographic evaluation might be considered if symptoms develop, and it reinforces the need for strict risk factor control (many PAD patients benefit from tighter glycemic control, foot care education, etc., in addition to standard cardiac care). Importantly, detection of PAD might also alter medical management; PAD patients may benefit from specific therapies (such as cilostazol for claudication, or newer antithrombotic regimes in select cases as per COMPASS trial using low-dose rivaroxaban plus aspirin for stable CAD/PAD) – though such therapies were beyond the scope of our study, they exemplify why identifying PAD is relevant.

Limitations:

This study has some limitations. First, the sample size (159) provides an estimate of PAD frequency with a moderate margin of error; a larger multicenter sample would yield more precise prevalence data. Second, our study population is from a single tertiary care center and may not fully represent the general CAD/ACS patient population in the community, especially in rural settings. There may be referral bias in our sample (possibly more severe ACS being referred and included). Third, we focused primarily on the presence of PAD via ABI and did not collect detailed data on PAD severity (e.g., specific ABI values or duplex ultrasound) or long-term outcomes. We also did not record some cardiovascular risk factors in all patients, which limits analysis of predictors of PAD within our cohort. Despite these limitations, our study provides valuable baseline data on the burden of peripheral arterial disease in ACS patients in Pakistan.

Future Directions:

Further research could extend these findings by following ACS patients with and without PAD longitudinally to assess differences in outcomes (reinforcing the prognostic impact of PAD in our population). It would also be useful to evaluate the effect of implementing routine ABI screening in cardiac units – for example, whether it leads to improved risk factor management or referral and if that translates into better outcomes. Additionally, studies exploring the utility of more advanced techniques (like arterial Doppler ultrasound or CT angiography of peripheral arteries) in high-risk ACS patients could be informative, although ABI remains the most practical initial tool.

Conclusion:

In conclusion, our study demonstrates that a meaningful proportion of patients presenting with acute coronary syndrome – about 7% in our cohort – have concurrent peripheral arterial disease when screened with the ankle-brachial index. Most of these cases are asymptomatic and would not have been recognized without active screening. Patients of older age are particularly likely to exhibit this coexistence of PAD and CAD. These findings highlight the systemic nature of

atherosclerosis in ACS patients and underscore the importance of a comprehensive approach to their care. Routine ABI screening in ACS patients, especially those above 60 or with multiple risk factors, should be considered as it can identify individuals at heightened risk for future cardiovascular events and allow clinicians to implement targeted preventive strategies. Ultimately, recognizing and treating PAD in patients with CAD can contribute to better overall cardiovascular outcomes and should form part of secondary prevention efforts in high-risk cardiac patients.

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