RESEARCH ARTICLE

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Categorization of acute coronary syndrome patients according to GRACE score and initial pulse pressure

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ABSTRACT **Background:** In emergency rooms and other clinical environments, acute coronary syndrome (ACS) is among the most often encountered Patient mortality from ACS is influenced by several risky variables. Among the prognostic markers, pulse pressure—which reflects the pulsatile element of blood pressure and is defined as the difference between systolic and diastolic blood pressure—has proven to be a practical and simple accessible clinical indicator. Pulse pressure, in contrast to static measures like systolic, diastolic, or mean arterial pressures, reveals cardiac function and vascular compliance. In this investigation, the GRACE score—a well-known instrument for predicting in-hospital mortality in ACS—was contrasted with pulse pressure in classifying ACS patients. **Objective:** This study's main goal is to investigate how ACS patients are classified according to pulse pressure and to analyze its prognostic value relative to the GRACE score, so highlighting pulse pressure's applicability and accessibility in medical environments. **Methods:** Using standard diagnostic criteria of clinical symptoms, ECG results, and cardiac enzyme levels, this study comprised 100 ACS-confirmed patients at IBN-SINA Teaching Hospital in Mosul. Through surveys and clinical evaluations, data were obtained. Based on pulse pressure, patients were divided into three groups: normal, narrow, and wide. For every participant, GRACE scores were computed. Exclusion criteria included disorders including congestive heart failure, valvular heart disease, endocarditis, severe anemia, thyrotoxicosis, chronic kidney disease, pregnancy, and athletic status that might influence pulse pressure. **Results:** Among the 74 men and 26 women in the study group, ages ranged from 30 to 89 years. Men were more often found to have abnormal pulse pressures. Among the 26 participants with narrow pulse pressure, 24 had wide pulse pressure; the rest had normal readings. With the wide pulse pressure group showing the highest creatinine levels, a very strong association ($p = 0.003$) between pulse pressure and serum creatinine levels was discovered. Wide pulse pressure was also strongly correlated with cardiac arrest and was linked significantly to higher systolic blood pressure measurements. STEMI was more prevalent than NSTEMI; neither wide nor narrow pulse pressure was linked with unstable angina. Patients with normal pulse pressure ($p = 0.037$) had more positive cardiac enzyme findings, but those with irregular pulse pressures also often showed positive results. While lower Killip classes were more frequent in the normal pulse pressure group ($p = 0.008$), narrow pulse pressure was linked with greater Killip class, signifying more severe heart failure. Moreover, while 72% of those with normal pulse pressure had lower GRACE scores, 50% of those with narrow pulse pressure were found to have high GRACE scores, indicating a very important link ($p = 0.007$). **Conclusion:** In individuals with acute coronary syndrome, pulse pressure demonstrated great predictive value. Both narrow and broad pulse pressures were shown in this investigation to be associated with negative clinical results. Emphasizing its possible part in risk stratification of ACS patients, narrow pulse pressure was strongly linked with greater GRACE scores and more strongly correlated with in-hospital mortality.

KEYWORDS acute coronary syndrome, pulse pressure, S. creatinine and grace score

1. INTRODUCTION

1.1 Acute coronary syndrome (ACS)

ACS is an umbrella term for ischemic myocardial disease including unstable angina (UA), non–ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarfection (STEMI).

For all practical reasons, UA and NSTEMI have different severity but same underlying pathophysiology [1]. A comprehensive assessment of clinical traits, electrocardiogram (ECG) results, and biochemical markers of myocardial necrosis underpins the diagnosis and categorization of ACS. UA is marked by ischemic symptoms without major biomarker elevations and by transient ECG changes. Myocardial infarction (MI) is defined as damage to the myocardium seen in acute myocardial ischemia. STEMI is distinguished from NSTEMI by the presence of ongoing ST-segment elevation ECG results. Particularly in relation to maximizing pharmacotherapy [2], advances have been achieved in ACS management recently.

1.2 Clinical presentation

Chest pain will afflict 20] to 40% of the general population over their lifetime. About 1.5 percent of the population see a primary care doctor yearly for signs of chest discomfort. In the emergency department—where chest pain accounts for over 5% of visits and as much as 40% of admissions—the rate is much higher [3].

All patients showing ischemic symptoms should be thought to have ACS. Ischemia manifests clinically as chest pain, upper extents, mandible, or epigastric discomfort, dyspnea, sweating, nausea, weariness, or fainting in several forms. Often widespread rather than localized, the agony and discomfort linked to an ACS incident could happen during activity or at rest. More often connected with MI is pain radiating to the left arm, right shoulder, or both arms, as is pain accompanied with diaphoresis. These symptoms are not particular for MI and do not appear in every patient having an ACS event. Unusual signs of ACS can arise in specific patient groups including women, the elderly, diabetics, or postoperative. ACS could be linked to palpitations, cardiac arrest, or an asymptomatic clinical presentation [2] in these cases.

1.3 Electrocardiogram

The single most crucial test in the first assessment of patients with ACS is a 12-lead electrocardiogram (ECG); it should be reviewed and performed within 10 minutes of arrival of a patient with suspected ACS. Presence of ST-segment elevation in two or more contiguous leads or a new left bundle branch block (LBBB) in the suitable clinical setting helps identify patients who would benefit from emergent reperfusion therapy. Transient ST-segment elevation, ST-segment depression, and/or T-wave inversions suggest a strong probability of ACS. These patients should be started on intensive medical treatment and assessed for early coronary angiography. Although a normal ECG lowers the risk of ACS, it is important to note that the posterior and lateral walls are not sufficiently reflected on the ECG and hence may not entirely rule out ischemia in those areas [4].

For leads V2 and V3, 1 mm for leads V1, V4-6, I, II, III, aVL, and aFL; and 0.5 mm for leads V3R and V4R (right-sided leads) and V7-9 (posterior leads), criteria to diagnose STEMI include ST segment elevation of 2 mm in men and 1.5 mm in women. Anatomically contiguous leads comprise either two precordial leads or two in an anatomic group. Elevated ST segments in leads II, III, and aVF might indicate a right ventricular infarct; hence, right-sided precordial or posterior leads should be acquired, particularly in a patient with clear lung fields but hypotension or jugular distention. Especially in cases of chest pain with raised cardiac troponin levels, a new or believed newly left bundle branch block indicates MI and calls for prompt treatment. Unless ischemia causes symptoms, a new left bundle branch block should not be viewed as an MI equivalent [3].

1.4 Pulse pressure

Defined as the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP), pulse pressure (PP) reflects the maximal and lowest blood pressures during the cardiac cycle.

Expected "normal" values for SBP and DBP are 120 mm Hg and 80 mm Hg, respectively, yielding an average PP of around 40 mm Hg. Physiologically, PP is seen as a reflection of vascular stiffness as well as stroke volume. Early systole sees the blood ejected from the left ventricle flow across large, elastic to narrow, muscular arteries throughout the arterial tree. Late systole creates a reflected wave against the LV that necessitates additional force generation (known as augmentation pressure) [5].

The differential diagnosis for a widened PP is extensive. Most usually seen in the setting of extensive cardiovascular disease, wide PP is a discrete predictor of disease progression and all-cause mortality [6].

PP is thought to be a surrogate for aortic stiffness; hence, the stiffer the aorta, the higher the PP. PP does, nevertheless, also show stroke volume and cardiac function. In the context of ACS, this dual meaning may be especially important since it might clarify inconsistencies in the existing research and offer a distinctive clinical instrument to assist stratify risk following diagnosis of ACS. Particularly, high PP (wide PP) could be a factor in causing plaque problems at coronary and cerebral levels. Conversely, a low PP (narrow PP) could assist find people at risk from major left ventricular malfunction [7].

Unlike the static measurements of systolic, diastolic, or mean arterial pressures, pulse pressure captures the pulsatile aspect of blood pressure. Extensive evidence have shown that post-myocardial infarction, in heart failure, and in ambulatory groups, pulse pressure might be a more reliable predictor than systolic, diastolic, or mean arterial pressures.

In the acute scenario, low pulse pressure could indicate restricted myocardial "reserve." By reducing coronary perfusion pressure and aggravating myocardial ischemia, high pulse pressure caused by a lowered diastolic component contrasts with normal conditions.

Particularly in patients older than 50 years of age, high pulse pressure is known to be independently linked to coronary artery disease risk in both normotensive and hypertensive individuals.

We sought to investigate the correlation between pulse pressure and clinical results throughout the wide range of non-ST-segment elevation ACS and STEMI, and to contrast its predictive usefulness [8].

Wide pulse pressure can be classified in terms of differential diagnosis into pathologic and physiologic origin. Advanced age, pregnancy, and well-conditioned athletes may be physiologic causes; pathologic differential diagnoses include atherosclerosis, aortic regurgitation, arteriovenous fistula, wet beriberi, distributive shock, elevated intracranial pressure, and hyperthyroidism/thyrotoxicosis [9].

Narrow pulse pressures arise in a number of conditions including cardiac failure (decreased pumping), blood loss (decreased blood volume), aortic stenosis (reduced stroke volume), and cardiac tamponade (decreased filling time). Most often, systolic pressures drop while diastolic pressures stay near normal [10].

1.5 GRACE score

Leading cause of mortality and morbidity worldwide is acute coronary syndrome (ACS). In patients with ACS—unstable angina (UA), non-ST-se-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI)—prospective risk stratification helps to guide angiography timing and so supports a tailored therapeutic approach. Major adverse outcomes in these patients can be predicted using the Global Registry of Acute Coron Syndrome risk score, which current American and European clinical recommendations advocate. Commonly employed in clinical practice to predict the risk of death or myocardial infarction—including in-hospital events—within six months, this risk stratification model comprising several clinical, laboratory, and electrocardiographic variables recorded on admission Furthermore, the latest recommendations for non-ST-elevation ACS patients suggest the GRACE score as a tool for detecting high-risk patients who will profit from an early invasive intervention [11].

Management of acute coronary syndrome depends critically on risk assessment [12]. The Global Registry of Acute Coronary Events score is now frequently employed as an acute risk stratification tool in the prognosis assessment of acute coronary syndrome patients [13]. Parameters of GRACE score include age, systolic blood pressure, heart rate, serum creatinine, Killip classification, cardiac arrest at admission, markers of myocardial necrosis, and ST-segment variations. Apart from their significant predictive value for both short- and long-term major adverse cardiovascular events, these eight independent prognostic risk factors also have predictive value for risk stratification and nosocomial adverse outcomes in patients with ACS. Guiding clinical diagnosis, therapy, and prognosis evaluation, the GRACE score is a whole assessment system. Still, it is not meant to define the complexity of CAD [14].

In patients with acute myocardial infaract (AMI), physical evaluation of left ventricular impairment is critical. Worsening Killip class is independently associated with increased mortality among patients with AMI. Society Guidelines for the evaluation of patients presenting with AMI [15] still today honor and advocate this classification system. Based on the Killip and Kimball criteria, patients are divided into four classes during physical examination. Patients in Class I show no signs of heart failure. Class II patients have results compatible with mild to moderate heart failure; Class III patients show clear pulmonary edema; Class IV patients are in cardiogenic shock [16].

2. PATIENTS AND METHODS

2.1 Study Design

A hospital-based cross-sectional study was carried out to achieve the aims of the study. One hundred patients diagnosed with acute coronary syndrome were recruited. The study was conducted in Mosul city at IBN-SINA Teaching Hospital over a period of six months, from 1st February 2021 to 1st August 2021.

2.2 Ethical Consideration

1. A formal consent was obtained from the Arabic Committee for Medical Specialization and the Scientific Council for Medicine of the Arabic Board.
2. A verbal consent was taken from the patients.

2.3 Exclusion Criteria

1. Patients with congestive heart failure, valvular heart disease, endocarditis, severe anemia, thyrotoxicosis, and chronic kidney disease.
2. Pregnant women and athletes.

2.4 Data Collection

Data were collected from patients during interviews using a checklist. After obtaining consent, the checklist was completed, and initial pulse pressure, heart rate, systolic and diastolic blood pressures were measured. Serum creatinine levels and cardiac enzymes were checked. ECG was performed for every patient. The Killip classification was used for risk stratification as follows:

- Killip class I includes individuals with no clinical signs of heart failure.
- Killip class II includes individuals with rales or crackles in the lungs, S3 gallop, and elevated jugular venous pressure.
- Killip class III describes individuals with frank acute pulmonary edema.
- Killip class IV describes individuals in cardiogenic shock or hypotension (measured as systolic blood pressure < 90 mmHg) and evidence of low cardiac output (oliguria, cyanosis, or impaired mental status).

The GRACE score was calculated for each patient and classified into three categories:

- Low risk: <109 points
- Intermediate risk: 109 to 140 points
- High risk: >140 points

It includes creatinine level, heart rate, systolic blood pressure, Killip class, age, cardiac arrest at admission, ST-segment deviation, and elevated cardiac enzyme levels.

Pulse pressure was calculated as the arithmetic difference between systolic and diastolic blood pressure on presentation.

Patients were divided into three groups according to pulse pressure:

- Narrow: <40 mmHg
- Normal: 40–60 mmHg
- Wide: >60 mmHg

2.5 Statistical analysis

Data were gathered and processed in Microsoft Excel (2007), then examined with the Statistical Package for Social Sciences (SPSS 26.0 for Windows). Shapiro-Wilk analysis found that the data followed normality, hence parametric tests were chosen. For numerical data, medians and quartiles were determined; for categorical data, proportions. To evaluate relationships and measure percentages between two groups, chi-square analysis was employed. When at least one cell had an expected value below 5, an alternative was Fisher's exact test. For continuous variables, the non-parametric Jonckheere–Terpstra test; for trends in categorical variables, the Mantel–Haenszel test evaluated differences across the three ordinal groups. Statistically significant was a p-value of ≤ 0.05.

3. DISCUSSION

About three-fourths of the patients enrolled in this study were male, and about one-fourth were female; this result is similar to a study conducted in India in 2013 by Mohanan et al. [17]. Additionally, the age of incidence of ACS in this study was close to that reported in the aforementioned article. The most affected age groups in our study were those between 50–59 years, followed by 60–69 years in both genders [17].

This study also shows that pulse pressure is higher in males than females, where 74 patients were male and 26 were female. Furthermore, wide pulse pressure was more common in older age groups compared to narrow pulse pressure, which was seen more in younger to older people. This finding is similar to the study conducted by Winston et al. [18] and corresponds with a 2015 study by Picher et al., which reported that pulse pressure amplification is lower in women than in men [19]. In that study, two-thirds of wide pulse pressure patients were male and one-third female, a pattern also seen in narrow and normal pulse pressures (73% and 78%, respectively).

In this study, heart rate showed no significant difference among pulse pressure types, with the average heart rate being the same in narrow and normal pulse pressure groups and slightly higher in the wide pulse pressure group. Pulse pressure abnormalities (narrow and wide) in relation to heart rate in patients with ACS are associated with poor outcomes. Narrow pulse pressure carries the worst outcome in relation to heart rate, consistent with findings from a 2018 study by Dobre et al. [20] and a similar result shown in a 2020 study by Yang et al. [21].

Creatinine levels were highest in association with wide pulse pressure, indicating that wide pulse pressure is associated with increased serum creatinine levels and may be a predictor of adverse kidney function. Similar results were reported by Tang et al. [10], as well as in studies by Safar et al. and Geraci et al. [22], [23]. This study also revealed that both wide and narrow pulse pressures were associated with elevated creatinine levels, but narrow pulse pressure was related to worse outcomes. Normal and narrow pulse pressures were associated with normal average creatinine readings. Pulse pressure is emerging as an important risk factor for end-organ damage and cardiovascular morbidity and mortality in many conditions.

Regarding systolic blood pressure, the highest readings were associated with wide pulse pressure compared to narrow and normal pulse pressures, consistent with findings by Christofaro et al. [24], although this was not statistically significant.

In this study, six patients developed cardiac arrest at admission; half of them had wide pulse pressure, one had narrow pulse pressure, and two had normal pulse pressure. This finding aligns with results reported by Tang et al. [7] and similar results shown by Homan et al. [25]. Of the remaining 94 patients who did not develop cardiac arrest, 48 had normal pulse pressure, and the rest (46 patients) were slightly more associated with narrow pulse pressure than wide pulse pressure.

Majority of patients with STEMI are associated with normal PP, followed by narrow PP and wide PP, but collectively STEMI occurs more in patients with abnormal PP, which is opposite to the result of Park et al. [26]. In patients with Non-STEMI, those with normal PP have the largest number compared to other pulse pressures, followed by wide PP and then narrow PP. This result is close to Park et al. [26], but opposite to the result of Tan et al. [27], which revealed a higher percentage of patients with Non-STEMI compared to STEMI in relation to wide PP. Neither wide PP nor narrow PP are associated with any patients with unstable angina; only a few patients with normal PP presented with unstable angina.

Most patients with narrow PP are associated with positive cardiac enzymes, as is also the case in wide PP patients, with 88.5% and 83.3%, respectively, which contradicts the findings of Tan et al. [27]. Only a few patients with both abnormal PPs had negative cardiac enzymes. Thirty-five of 50 patients with normal PP had positive cardiac enzymes, which is the largest number of patients associated with positive cardiac enzymes, while 15 of 50 had negative results [27].

This study shows a highly significant association between narrow PP and higher Killip class compared to other pulse pressure types.

- The majority of patients with Killip class 1 had normal PP, and most patients with normal PP are associated with Killip class 1. In contrast, patients with wide and narrow PP showed no large difference in the percentage of patients in relation to Killip class 1.
- Patients with Killip class 2 showed varying percentages: half of the patients with narrow pulse pressure had Killip class 2, one-third of patients with normal pulse pressure had Killip class 2, while about two-thirds of patients with wide pulse pressure were associated with Killip class 2. This suggests that the majority of patients with narrow PP are associated with increasing Killip class, while the majority of patients with wide PP are associated with Killip class 2. Both wide and narrow PP had similar numbers of patients associated with Killip class 2.

- The highest percentage of patients associated with Killip class 3 were those with narrow pulse pressure compared to other pulse pressure types, with 3 of 5 patients with Killip class 3 having narrow pulse pressure. This leads to the conclusion that abnormal PP, especially narrow PP, is associated with higher Killip class, indicating worse clinical outcomes [28], [29]. These results underscore the need to closely monitor such patients and urgently refer them for cardiac interventions to prevent further deterioration in those with Killip class > 2 and narrow pulse pressure, as the strong association between them is clear [30].

In this study, narrow and wide pulse pressures were associated with significant adverse events in patients with acute coronary syndrome:

- The results show that narrow pulse pressure is associated with the highest class of GRACE score compared to other pulse pressures. Two patients died in the CCU during data collection, both having high GRACE scores and narrow pulse pressures.
- Wide pulse pressure is associated with intermediate GRACE scores, which is also considered a poor outcome, as reported by Tang et al. [27]. This indicates that both pulse pressures carry worse outcomes for patients with ACS (wide pulse pressure carries high risk, while narrow pulse pressure has worse outcomes). These findings are consistent with the study by Park et al. [26]. Wide pulse pressure not only shows prognostic value in ACS patients but also reflects the degree of arterial stiffness. Similar findings were reported by Omer et al. (2014) and Tang et al. [31], where higher pulse pressure reflects more arterial stiffness and correlates with higher GRACE scores (intermediate).
- Patients with normal pulse pressure have the highest percentage of low GRACE scores, which aligns with the aim of this study, indicating that patients with normal PP have low-risk complications according to the GRACE score.

Our findings have direct and easy clinical applicability in daily practice, with the implicit recommendation for clinicians to consider pulse pressure in addition to systolic and diastolic blood pressure, a practice not yet very common [32].

4. CONCLUSION

Pulse pressure was a strong prognostic measure in ACS patients. In this study, we found that narrow and wide pulse pressures are associated with significant adverse events in patients with acute coronary syndrome. Narrow pulse pressure is associated with a higher class of GRACE score and is more strongly linked to intra-hospital mortality. Wide pulse pressure carries high risk, while narrow pulse pressure is associated with worse outcomes.

5. RECOMMENDATION

1) Use pulse pressure as an initial indicator and prognostic measurement in ACS patients.
2) Further studies with larger samples are needed to verify the relationship of pulse pressure with serum creatinine, acute kidney injury, and cardiac arrest.
3) Further studies with larger samples are needed to verify the correlation of narrow pulse pressure with acute heart failure in ACS patients.
4) Further studies with larger samples are needed to verify the relationship of unstable angina with abnormal pulse pressure.

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