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Relevance of GENSINI Score in Acute Coronary Syndromes

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Abstract:

Background: Guidance on the diagnostic approach to coronary artery disease (CAD) has diverged as the increasing complexity of atherosclerotic clinicopathologic correlations has been revealed. Foundational concepts linking stenosis, the ischaemic cascade and prognosis have been re-evaluated in light of the underwhelming results from the percutaneous revascularization of stenotic vessels. Instead, observations from noninvasive anatomical imaging have redefined risk, shifting the focus away from discrete lesions towards total atherosclerotic burden, and with it elevating the role of computed tomography (CT) in contemporary diagnostic pathways. Quantitative determination of atherosclerosis by Gensini score (GS) may be as important as other risk-factors for disease management. Angiographic scoring systems are strongly correlated with each other and with atherosclerotic plaque burden. Therefore, scoring systems appear to be a valid estimate of CAD plaque burden. **Objective**: This review article aims to role of GENSINI score in assessment CAD severity. **Conclusions**: GS were correlated to the severity of coronary lesions, especially with multivessel disease, CABG and implanted LIMA or drug eluting stent. GS reflecting severity of atherosclerosis is related to several cardiovascular risk factors, such as age, HDL, HTN, and diabetes. GS can provide valuable information about the severity and prognosis of CAD. Using GS to assess angiographic severity of CAD is potentially useful for predicting patient outcomes and benefit of therapies and can improve the quality of care.

Keywords:GENSINI Score; CAD, STEMI.

1. Introduction

It is well-known that the cardiovascular diseases (CVD) are the leading cause of deaths all over the world. In particular, coronary artery diseases (CAD) are the major cause (43.8%) of deaths attributable to CVD in the United States. Give this, percutaneous coronary intervention (PCI) is becoming the most popular treatment for CAD. While there have been technical advances in the PCI process, there is still a high incident rate of periprocedural myocardial infarction (PMI) rate of approximately 5% to 30% continues to be reported.

Therefore, it is critical that clinical practitioners discover a unique predictor for the presence of PMI as a significant orientation in the cardiology field **(Wang et al., 2022)**.

The Gensini score (GS) is a convenient and powerful tool for assessing the severity and complexity of narrowing in the coronary arteries, as are the SYNTAX score,American Heart Association (AHA)/American College of Cardiology (ACC) classification,and LEAMAN score**(Sianos et al., 2005)**.

In the past few decades, GS has played a key role in the description of CAD degree. In addition, GS may also be used to stratify risk for long-term prognosis. While many authors consider GS a primary outcome for evaluating the severity of CAD before PCI, a few authors have explored the relationship between GS and after-procedural complications, in particular PMI **(Chen et al., 2017)**.

At present, a number of studies have confirmed that the Gensini score can predict the risk of major adverse cardiovascular and cerebrovascular events (MACCEs) in patients with different types of CAD and evaluate the severity of coronary artery lesions combined with certain biochemical indicators. However, there are few studies related to the outcomes after PCI, especially the reports on the long-term outcomes. thophysiologic basis of myocardial necrosis after PCI**(Wang et al., 2021)**.

This review aimed to determine therole of GENSINI score in assessment CAD severity.

2. The Gensini scoring system

Gensini score (GS) provides valuable information on severity and prognosis of coronary artery disease (CAD). Gensini score is an effective tool used to evaluate the severity of coronary artery disease (CAD)**(Aksu and Ahmed, 2024)**.

Gensini score GS was used to evaluate the severity of atherosclerosis. The most severe stenosis in each of the 8 coronary segments was graded from 1 to 4 (1%-49% lumen diameter reduction: 1 point; 50%-74% stenosis, 2 points; 75%-99% stenosis, 3 points; and 100% occlusion 4 points) to give a total score of 0 to 32. This score provides an index of the severity of coronary atherosclerosis. Coronary thrombus was defined as a filling defect surrounded by contrast media in the absence of calcification and dissection**(Charach et al., 2021)**.

Total occlusion was defined as the absence of any anterograde opacification. Coronary calcification was defined as the visualization of any coronary calcified lesion viewed by angiography. The Gensini scoring system was used to evaluate CAD severity. The GS was calculated for each patient from the coronary arteriogram by assigning a severity score to each coronary stenosis according to the degree of luminal narrowing and its geographic importance. Decreased lumen diameter and the roentgenographic appearance of concentric lesions and eccentric plaques were evaluated (reductions of 25%, 50%, 75%, 90%, 99%, and complete occlusion were given GS of 1, 2, 4, 8, 16, and 32, respectively)**(Sinning et al., 2013)**.

The Gensini score is a better indicator of the total atherosclerotic load because it looks at lesions with as little as 25% luminal stenosis. This is different from the SYNTAX score, which does not include occlusive lesions with less than 50% stenosis. Additionally, according to intracoronary ultrasonography results, the Gensini score significantly correlates with both the average plaque burden and the plaque area. On the other hand, in individuals with CCS, both Gensini and SYNTAX scores have a small predictive value for the occurrence of cardiovascular events(**Matos et al., 2021**).

Combining these scores improves their predictive value, especially for lower-risk scores. In another study using GS, the CAD group was divided into two groups for the purpose of predicting severe CAD. The cut-off value was 7.45%, resulting in a sensitivity of 58.8% and a specificity of 67.2%(**Blaum et al., 2021**).

Calculation of the Gensini score was initiated by giving a severity score to each coronary stenosis as follows: It defined narrowing of the lumen of the coronary arteries as 1 for 1 to 25% stenosis, 2 for 26 to 50%, 4 for 51 to 75%, 8 for 76 to 90%, 16 for 91 to 99%, and 32 for total occlusion. The score was then multiplied by a factor representing the importance of the lesion location in the coronary artery system. For the location scores, 5 points were given for a left main lesion; 2.5 for the proximal left anterior descending (LAD) or left circumflex (LCX) artery; 1.5 for the mid-segment LAD and LCX; 1 for the distal segment of the LAD and LCX, first diagonal branch, first obtuse marginal branch, right coronary artery, posterior descending artery, and intermediate artery; and 0.5 for the second diagonal and second obtuse marginal branches **(Avci et al., 2016).**

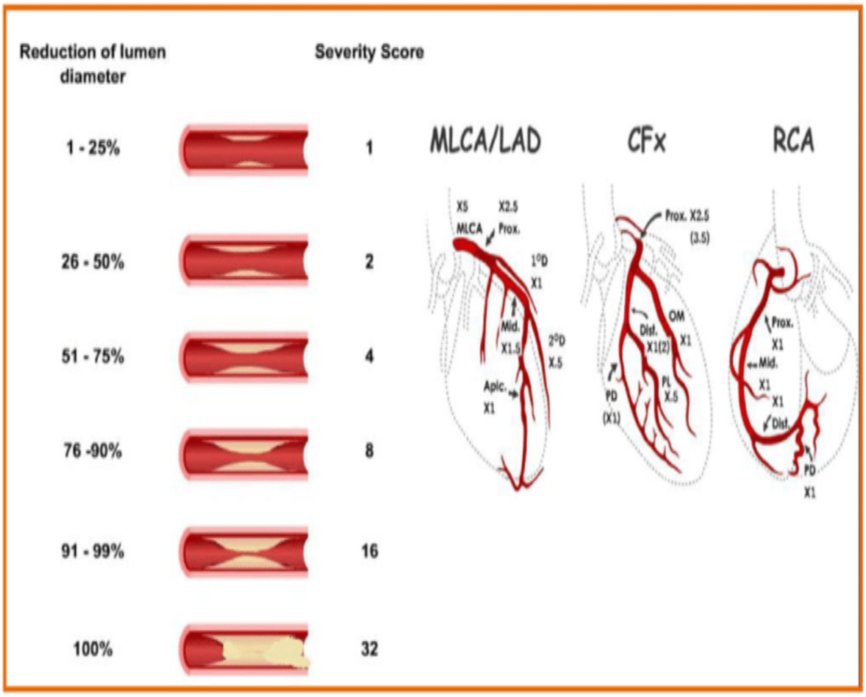

Figure 2: How to calculate Gensini score (Kamal et al., 2018)

The severity of CAD was evaluated by the Gensini score assessment system and scored by two independent senior cardiologists. The degree of stenosis and the coronary artery lesion site were scored as follows: 1 point for ≤ 25% narrowing, 2 points for 26–50% narrowing, 4 points for 51–75% narrowing, 8 points for 76–90% narrowing, 16 points for 91–99% narrowing, and 32 points for total occlusion. Thereafter, each lesion score is multiplied by a factor that takes into account the importance of the lesion's position in the coronary circulation (5 for the left main coronary artery, 2.5 for the proximal segment of the left anterior descending coronary artery, 2.5 for the proximal segment of the circumflex artery, 1.5 for the mid-segment of the left anterior descending coronary artery, 1.0 for the right coronary artery, the distal segment of the left anterior descending coronary artery, the posterolateral artery, and the obtuse marginal artery, and 0.5 for other segments)**(Wang et al., 2021)**.

Finally, the Gensini score was calculated by summation of the individual coronary segment scores. The patients were classified into three groups according to the tertile of Gensini score: first tertile (Gensini score <11 points), second tertile (Gensini score 11–38 points), third tertile (Gensini score >38 points)**(Yokokawa et al., 2020)**.

3. Using the Gensini score to estimate severity of STEMI, NSTEMI, unstable angina

Non-ST-segment elevation myocardial infarction (NSTEMI) is one of the leading causes of morbidity and mortality, and accounts for high healthcare costs worldwide. The Gensini scoring system, based on angiographic findings, is a valuable method for estimating the severity of coronary artery disease. The severity of coronary artery lesions, as assessed by the Gensini score (GS), is associated with long-term mortality and major adverse cardiac event rates**(Zhenhong et al., 2012)**.

Gensini score (GS) was introduced in 1983and is used for determining CCS severity based on changes in the lumen segment, stenosis degree, and coronary stenosis site. Research has confirmed the crucial value of GS in assessing CCS condition **(He et al., 2021)**, and it is an independent predictor of long-term adverse outcomes in patients with CCS who have undergone percutaneous coronary intervention (PCI) **(Wang et al., 2021)**.

A retrospective study found the GS of patients with CCS to be significantly different from that of healthy individuals; furthermore, statistical analysis showed a correlation between GS and patient prognosis**(He et al., 2021)**. Nevertheless, the relationship between GS and ET-1 and NO serum levels in patients with CCS needs elucidation.

STEMI/NSTEMI and UAP were related to more extensive and complex coronary lesions in patients with coronary atherosclerosis. The extent of CAD was based on quantitative determination of atherosclerosis, as expressed by GS**(Celik et al., 2013)**.

Patients with NSTEMI in contrast to STEMI and UAP had higher GS of coronary arteries. This finding may be because most NSTEMI patients were older and sicker than STEMI or UAP patients were**(Tanaka et al., 2021)**.

Marked differences in GS between patients who underwent PCI after CABG (and separately for LIMA and SVG) and those who did not have CABG and LIMA or SVG implantation can be explained by an active atherosclerotic process and oxidative stress in non-native vessels**(George et al., 2000)**.

Patients with only chest pain and inconclusive stress test (thallium scan, stress ECHO or treadmill ergometry) had the lowest GS.

GS was well-correlated with age, total cholesterol and HDL, and DM. The highest GS was found in patients with DM because most had CAD and dyslipidemia. The question as to why Spearman correlations were not significant between GS and cardiac risk factors such as HTN, smoking, troponin, BMI, and waist circumference remains unclear. However, it may be because the patients were treated for various risk-factors, both medically and by life-style changes. A large diabetes trial did not find any relation between symptoms and disease severity for women or men with DM(**Tamis-Holland et al., 2011**).

There were no differences in GS between smokers and nonsmokers and between the patients with BMI above or below 25 (P=.06) and in patients with and without HF or CVA. This can be explained by preventive treatment for several risk-factors. GS of patients with various risk-factors but without acute myocardial infarction (STEMI and NSTEMI) were similar by approximately 68 to 71 score (P>.05)(**Charach et al., 2021**).

For patients who manifest ST-segment elevation diagnostic for STEMI, emergent reperfusion therapy remains the immediate priority, as emphasised in the most recent European and American guidelines. The latest data continue to reinforce the association between prompt (<90 min) reperfusion and more favourable long-term clinical outcomes. Patients presenting to a percutaneous coronary intervention (PCI)-capable hospital should undergo immediate coronary angio-graphy with a goal of first medical contact-to-device time of less than 60–90 min **(Sousa-Uva et al., 2019).**

For patients presenting to a non-PCI centre, transfer to PCI should be executed if the anticipated time to PCI will be 120 min or less. Alternatively, if PCI within this timeframe is not possible, fibrinolysis should be administered if not contraindicated, and a pharmaco-invasive approach should be considered in which initial fibrinolytic therapy is followed by invasive angiography within 24 h **(Fazel et al., 2020).**

About half of patients with STEMI have obstructive coronary disease outside the infarct-related artery, and the presence of flow-limiting non-infarct-related artery lesions portends a worse prognosis. The COMPLETE trial of 4041 patients with hemodynamically stable STEMI and at least one other significant non-culprit lesion found that patients randomized to complete revascularization of all lesions within 45 days resulted in a lower rate of cardiovascular death or myocardial infarction compared with culprit-only PCI **(S. R. Mehta et al., 2019).**

The COMPLETE trial built upon several smaller trials suggesting potential benefit with complete revascularization and a meta-analysis of complete versus culprit-only revascularization in haemo dynamically stable STEMI found a significantly lower rate of cardiovascular death in patients assigned to complete revascularization **(Bainey et al., 2020).**

ESC guidelines 2023 recommend complete revascularization either during the index PCI procedure or within 45 days **(Bainey et al., 2020).**

Importantly, the COMPLETE trial findings cannot necessarily be extended to patients with acute myocardial infarction (STEMI or NSTEMI) complicated by shock. In the CULPRIT-SHOCK trial, 706 patients with acute myocardial infarction with shock and significant non-culprit coronary lesions were randomised to multivessel PCI at the time of the index to culprit lesion-only PCI **(Thiele et al., 2017).**

Patients assigned to immediate multivessel PCI had higher rates of renal failure and death than did those assigned to culprit lesion- only PCI. Based on the CULPRIT-SHOCK trial, routine immediate non-culprit lesion PCI is not recommended in these patients. Whether staged revascularisation after resolution of the shock and concomitant end-organ injury may be beneficial is not currently known **(Collet et al., 2021).**

4. Role of GENSINI score in assessment CAD severity

The Gensini score is a comprehensive angiographic score that reflects the magnitude of coronary atherosclerotic disease burden. Although this method is not perfect, it provides more relevant information than just categorising patients as single, double, or triple. The following are considered to be the benefits of this scoring approach: It accurately stratified patients based on the functional relevance of their condition; it provides for continuous, microprocessor-assisted interobserver investigations as well as intraobserver variability **(Gensini, 1983, Aksu and Ahmed, 2024)**.

The Gensini scoring system is an objective method to determine the severity of CAD according to angiographic findings. It was originally developed to quantify the severity of CAD. Gensini score fully considers the number, location, and degree of stenosis of coronary artery lesions, which is a more scientific evaluation standard of coronary artery lesions **(Gensini, 1983).**

Currently, there are a variety of scoring systems used for quantitative analysis of coronary artery lesions and Gensini scoring is more commonly used in clinical practice. Gensini score fully considers the number, location, and degree of stenosis of coronary artery lesions, which is a more scientific evaluation standard of coronary artery lesions **(Wang et al., 2021)**.

At the same time, this scoring system has also been widely used in related studies on the clinical outcomes of CAD. At present, a number of studies have confirmed that the Gensini score can predict the risk of major adverse cardiovascular and cerebrovascular events (MACCEs) in patients with different types of CAD and evaluate the severity of coronary artery lesions combined with certain biochemical indicators**(Duran et al., 2012).**

GS is an easy-to-use and powerful tool for assessing coronary arteries stenosis severity and complexity. GS is used to assess stenosis severity. The etiopathogenesis of coronary stenosis is mainly atherosclerosis. The lesion starts from the intima damage, and several types of lesions, including accumulation of lipids and complex sugars, fibrous tissue hyperplasia, and calcification, and gradual degeneration of the middle layer of the artery, occur(**Michelis et al., 2021**).

In the past few decades, GS has found widespread application to assess the degree of CCS severity. An observational study reported that GS values can predict periprocedural myocardial infarction. Moreover, another study found that GS is an independent predictor of long-term adverse outcomes in patients with CCS who underwent PCI(**Wang et al., 2022**).

The Gensini score is a better indicator of the total atherosclerotic load because it looks at lesions with as little as 25% luminal stenosis. This is different from the SYNTAX score, which does not include occlusive lesions with less than 50% stenosis. Additionally, according to intracoronary ultrasonography results, the Gensini score significantly correlates with both the average plaque burden and the plaque area **(Blaum et al., 2021)**.

On the other hand, in individuals with CCS, both Gensini and SYNTAX scores have a small predictive value for the occurrence of cardiovascular events. Combining these scores improves their predictive value, especially for lower-risk scores **(Kilic et al., 2020)**.

Risk factors are associated with the occurrence of atherosclerosis, but not with the prevalence and severity of atherosclerosis. The Gensini score accurately predicts the severity of coronary artery disease in the Somali patient population and can guide treatment decisions **(Aksu and Ahmed, 2024)**.

Using these scores alone is not enough; therefore, to improve the prediction of coronary artery disease and select the appropriate therapy, it is important to combine angiography with available risk factors such as arterial hypertension, smoking, diabetes, etc **(Nissen et al., 2018)**.

5. Gensini Score and In-Hospital course in Patients with ST-Segment Elevation Myocardial Infarction.

Although primary percutaneous coronary intervention (P-PCI) has been contributing to a decrease in mortality in recent years, ST-segment elevation myocardial infarction (STEMI) is still one of the leading cause of mortality and morbidity all over the world. In-hospital mortality rates were reported as 7-10% in some registries. Currently, several validated risk factors and scoring systems are used to predict mortality in STEMI patients(**Araszkiewicz et al., 2013**).

In the fibrinolytic era, thrombolysis in myocardial infarction (TIMI) risk score was developed as a clinical risk score to predict 30-day mortality in patients with STEMI. TIMI score was derived and validated among fibrinolytic-eligible patients enrolled in clinical trials, so it cannot be easily applied in STEMI patients undergoing P-PCI. Recently, the Global Registry of Acute Coronary Events (GRACE) score has been defined for predicting mortality at 6 months in patients with acute coronary syndromes (ACS), but critically ill patients such as those who died early may be underrepresented(**Fox et al., 2006**).

In addition to these clinical scores, some coronary angiography-based scoring systems such as Gensini, SYNTAX (synergy between percutaneous coronary intervention with Taxus and cardiac surgery) and ACC/AHA have been established to assess the severity of lesions and provide some prognostic information for patients with coronary artery disease (CAD). Although these scoring systems provide quantitative evaluation, the valuable detailed information derived from angiography is not sufficiently used. In clinical practice, there is a need for an initial stratification of STEMI patients, which aims to identify those at higher risk and decrease the incidence of major adverse cardiovascular events through more appropriate targeting of preventive measures(**Boyraz and Peker, 2022**).

The Gensini scoring system is an objective method to determine the severity of CAD according to angiographic findings.5 It was originally developed to quantify the severity of CAD; however, subsequent studies have demonstrated its ability to identify patients who are at high risk of adverse events who are treated with PCI(**Neeland et al., 2012a**).

However, little is known about the association between the severity of CAD assesed by the Gensini score and in-hospital mortality in patients with STEMI undergoing P-PCI(**Yıldırım et al., 2017**).

Briefly, the diagnosis of STEMI was made through the criteria of classical symptoms of coronary ischemia (chest pain lasting > 30 minutes), detection of > 1 mm ST-segment elevation in at least two contiguous leads and elevation in cardiac biomarkers, and defined by the guidelines of the American College of Cardiology and the European Society of Cardiology(**O'Gara et al., 2013**).

The severity of CAD was calculated using the Gensini score, in which the calculation is based on the evaluation of the number of stenotic segments along with their respective degrees of luminal narrowing and localization within the coronary tree(**Avci et al., 2016**).

STEMI is the most important part of ACS. Consistently with our data, in-hospital mortality rates ranged between 6% and 14%. Many factors such as previous MI, door to balloon time, presence of diabetes, anemia, chronic renal failure, and ejection fraction on admission are known to be predictors of mortality in this era. To date, several validated patient-based risk scores such as TIMI, GRACE, ZWOLLE, CADILLAC and PAMI have been established for predicting mortality and morbidity in patients presenting with STEMI(**Esenboğa et al., 2021**).

Most of these scores were based on clinical parameters such as age, gender, Killip class, serum creatinine levels, and degree of ST-segment change. This is not surprising, as these scores were developed before the widespread adoption of P-PCI for STEMI. TIMI and GRACE scores are valuable tools for initial risk stratification of STEMI patients. TIMI is widely accepted due to its ease of use. Despite its good predictive power, the GRACE score has limited bedside use because of the necessity to use specialized computer software and graphs. These scores were not specifically optimized for patients with STEMI undergoing P-PCI(**Zhao et al., 2022**).

In the P-PCI era, some of the scoring systems such as CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications),12 Stent-PAMI (Stent-Primary Angioplasty in Myocardial Infarction),and MCRS (The Mayo Clinic Risk Score) included angiographic variables in the scoring algorithm. The CADILLAC risk score was able to accurately predict 30-day and 1-year mortalities after P-PCI in STEMI patients. Baptista et al. applied the PAMI risk score to a small population of STEMI patients and revealed that this method was able to predict in-hospital, 30-day and 6-month mortality. The MCRS is also a validated risk model for pre-procedure risk stratification and has been showing a good capacity for the prediction of in-hospital mortality**(Baptista et al., 2004)**.

In addition to those scores, which were established from combination of both clinical and angiographic variables, some scoring systems based solely on angiographic data such as SYNTAX are associated to short and long-term follow-up in patients with STEMI undergoing P-PCI(**Sianos et al., 2005**).

The purpose of coronary scoring systems is to quantify the severity of coronary stenosis. Different coronary arteries carry different volumes of blood to the heart, and coronary scores take this into account. The degree of stenosis was also considered in these scoring systems. Overall, the individual ability of these angiography-based scores to predict mortality is uncertain, and an important limitation is that these scores have been largely limited to elective patients.Although the SYNTAX score is frequently used for predicting mortality in patients with STEMI undergoing P-PCI, the percent diameter stenosis is not considered in scoring and a distinction is made only between occlusive (100%) and non-occlusive (50-99% stenosis) disease**(Neeland et al., 2012b)**.

Furthermore, stenosis is considered severe when it causes ≥ 50% reduction in the luminal diameter by visual assessment in vessels ≥ 1.5 mm. However, in the Gensini score, lesions causing < 50% reduction in the luminal diameter in vessels < 1.5mm diameter are considered in the scoring algorithm. The Gensini score was originally developed to quantify the severity of CAD. It has been widely used in clinical trials to assess the extent and severity of CAD. However, subsequent studies have demonstrated its ability to identify patients treated by PCI who are at high risk of adverse events. Nevertheless, little is known about the correlation between the Gensini score and short-term mortality in STEMI patients(**Acet et al., 2015**).

There are few recently published studies that have evaluated the Gensini score in the context of P-PCI. In a recent report, the Gensini score was found to be associated with lower MACE during hospital stay and at 6 months after PCI in acute STEMI patients.24 Thus, the authors concluded that it could be used to predict short-term MACE in STEMI patients during the post PCI period. Acet et al.25 found that the TIMI risk index is significantly related to the

Gensini score in predicting the extent and severity of CAD in patients with STEMI(**Qin et al., 2015**).

6. Conclusions:

GS were correlated to the severity of coronary lesions, especially with multivessel disease, CABG and implanted LIMA or drug eluting stent. GS reflecting severity of atherosclerosis is related to several cardiovascular risk factors, such as age, HDL, HTN, and diabetes. GS can provide valuable information about the severity and prognosis of CAD. Using GS to assess angiographic severity of CAD is potentially useful for predicting patient outcomes and benefit of therapies and can improve the quality of care.

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