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REVIEW ARTICLE

Prognostic Value of The Leuko-Glycemic Index in Acute Myocardial Infarction; a Systematic Review and Meta-Analysis

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Abstract: **Introduction:** In recent years, studies have provided evidence on the prognostic value of the leuko-glycemic index (LGI) in acute myocardial infarction (MI), but there is a lack of consensus. In addition, various reported cut-offs for LGI have raised concern regarding its clinical applicability. So, to conclude, through this systematic review and meta-analysis, we aimed to investigate all available evidence on the prognostic value of LGI in acute MI. **Methods:** Two independent researchers summarized records available in the four main databases of Medline (Via PubMed), Embase, Scopus, and Web of Science until 15 Sep 2022. Articles studying the prognostic value of the LGI in acute MI were included. Finally, sensitivity, specificity, prognostic odds ratio, and the area under the curve (AUC) for LGI were analyzed and reported. **Results:** Eleven articles were included (3701 patients, 72.1% male). Based on the analyses, AUC, sensitivity, and specificity for LGI in prediction of mortality following acute MI were 0.77 (95% CI: 0.73 to 0.80), 0.75 (95% CI: 0.62 to 0.84), and 0.66 (95% CI: 0.51 to 0.78), respectively. Positive and negative post-test probability of LGI in prediction of mortality were 21% and 5%, respectively. AUC, sensitivity, and specificity for LGI in prediction of major cardiac complications after acute MI were 0.81 (95% CI: 0.77 to 0.84), 0.84 (95% CI: 0.70 to 0.92), and 0.64 (95% CI: 0.49 to 0.84), respectively. Also, the Positive and negative post-test probability of LGI in this regard were 59% and 13%, respectively. **Conclusion:** Although the results demonstrated that the LGI could predict mortality and acute cardiac complication after MI, the low post-test probability of LGI in risk stratification of patients raises questions regarding its applicability. Nevertheless, as most of the available studies have been conducted in the Latino/Hispanic population, further evidence is warranted to generalize the validity of this tool to other racial populations.

Keywords: Glycemic index; prognosis; acute coronary syndrome; myocardial ischemia; death; myocardial infarction

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1. Introduction

Cardiovascular disease stands as the leading cause of death worldwide. The latest estimates in 2019 revealed an incidence of 523 million cardiovascular events, accounting for more than 18 million deaths and causing 32% of mortalities, globally. More than 75% of cardiovascular mortality is reported in middle- and low-income countries, with myocardial infarction (MI) being the etiology in about half of cases (1, 2).

Identifying high-risk patients with poor prognoses suffering

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from ischemic heart disease can assist physicians in providing the most appropriate care and implementing preventive measures (3, 4). Utilizing blood biomarkers and decision tools has been demonstrated to be promising in the risk stratification of patients (5-10). The temporal profile of inflammatory markers released as the primary systemic response to ischemic heart disease can be helpful in diagnosing and estimating the severity of the ischemic injury. In this regard, multiple studies have revealed that increased concentration of specific inflammatory biomarkers is associated with the outcome of patients following acute MI (11-13). However, low specificity, high cost, and unavailability of these biomarkers in some settings, hinder their clinical applicability.

In 2010, Quiroga Castro et al. introduced the leuko-glycemic index (LGI) as a prognostic model for acute MI (14). Synthesized through multiplying blood glucose level by leukocyte count, the LGI gained popularity for risk stratification of MI patients (15-17). The simplicity of calculation and routine measurement of involved variables on admission among MI patients made the leuko-glycemic index an accessible and easily interpretable test with no significant costs for patients and health systems.

Although, in recent years, studies have been conducted to validate the prognostic value of LGI among acute MI patients, there is still a lack of consensus (15-19). Furthermore, the diversity of reported cut-offs among studies results in difficulty and uncertainty in the clinical use of this index. So, intending to determine the prognostic value of this index in acute MI patients, we ran a systematic review and meta-analysis of all available studies in the literature.

2. Methods

2.1. Study design

The present systematic review and meta-analysis comprehensively explored all available studies on the prognostic value of the LGI among acute MI patients. Based on the study aims, the PICO has been defined as follows:

P (population): patients with acute myocardial infarction

I (intervention): the leuko-glycemic Index

C (comparison): comparison with the non-outcome group

O (outcome): mortality and major cardiac complications

The protocol of the current meta-analysis was registered in the online management systems of research project for Shahid Beheshti University of Medical Science. The local ethics committee approved the protocol of the current meta-analysis (IR.SBMU.RETECH.REC.1401.533).

2.2. Search strategy

In the beginning, relevant keywords were selected by experts in this field. Emtree and MeSH databases were extensively explored to find synonyms and other keywords. In addition, the title and abstract of related articles were screened to explore further keywords and synonyms. Ultimately, using the acquired keywords, a comprehensive search in online databases of Medline (via PubMed), Embase, Scopus, and Web of Science was conducted until Sep 15, 2022. Besides the systematic search, a manual search was performed on Google, Google Scholar, and Semantic Scholar search engines for preprints and other probable records not found during the systematic search. We didn't apply any language restrictions for selecting studies. The search queries of all explored databases are provided in supplementary material 1.

2.3. Selection criteria

Inclusion criteria consisted of human studies on prognostic value of LGI in acute MI patients, published in peer-reviewed journals, which calculated the leuko-glycemic index for risk stratification. Studies on patients with other chief complaints rather than acute MI such as heart failure and COVID-19, reporting data or patients undergoing surgical interventions such as coronary artery bypass graft (CABG) and other cardiac surgeries, studies without primary outcome measurements or existence of the outcomes at baseline were excluded. The other exclusion criteria were animal studies, duplicated studies, retracted or withdrawn studies, reviews, and case reports.

2.4. Screening and data collection

Records collected through systematic and manual searches were exported to Endnote software version 19.0 (Clarivate Analytics, Philadelphia, PA, USA), and duplicates were removed.

Two independent reviewers screened the titles and abstracts of studies and retrieved the full texts of possibly related articles. Then, based on the predefined inclusion and exclusion criteria, eligible articles were included in the present study. Reviewer disagreements were addressed through discussion and consultations with a third expert. Reporting data on study characteristics (first author name, publication and study year, country), type of study, sample size, age and gender distribution, reported outcomes, the timing of blood glucose and leukocyte measurements, reported cut-offs for the LGI, prognostic value indicators like sensitivity, specificity, and false and true positives and negatives (FP, TP, FN, TN) were extracted. Before the study initiation, we considered collecting odds ratio (OR), hazard ratio (HR), relative risk (RR), and the area under the curve (AUC) of LGI in prognostication of acute MI in patients. However, we didn't enter these values in our meta-analysis due to few studies reporting the above data and the inability to do pooled analysis on HR, OR, and RR of included studies.

Table 1: Characteristics of included articles

Study	Data	Study design	Language	Sample size	Mean age	Male (n)	Timing of LGI (hrs)	Patients setting	Outcome	Cut off of LGI	TP	TN	FP	FN
Cuesta-Mero, 2021, Ecuador	2015 to 2016	PCS	Spanish	205	62.99± 12.2	142	24	ST- and non-ST-elevated MI	In-hospital mortality	851.6	23	116	65	1
									In-hospital MCC (cardiac arrest, HF, cardiogenic shock, severe dysrhythmia, re-MI, ventricular thrombus, angina)	656.8	117	42	17	6
Diaz Benitez, 2016, Cuba	2012 to 2013	Cross	Spanish	142	68.2± 10.3	83	24	ST- and non-ST-elevated MI (all patients)	30-day mortality	1443	16	19	2	3
								ST- and non-ST-elevated MI (non-diabetic patients)	30-day MCC	1443	28	56	17	1
								ST- and non-ST-elevated MI (diabetic patients)	30-day MCC	1443	16	19	2	3
Hirschson Prado, 2014, Argentina	2011	PCS	English	405	61±12	348	8	ST-elevated MI	In-hospital mortality	738	23	53	329	0
									In-hospital mortality	975	17	184	198	6
									In-hospital mortality	1401	13	301	81	10
									In-hospital MCC (Cardiac death and HF)	738	50	53	302	0
									In-hospital MCC (Cardiac death and HF)	975	40	180	175	10
									In-hospital MCC (Cardiac death and HF)	1401	29	290	65	21
Leon-Aliz, 2014, Cuba	2009 to 2010	RCS	Spanish	128	68± 11.5	96	24	ST-elevated MI	In-hospital mortality	1158	11	90	24	3
									In-hospital MCC (cardiac arrest, HF, cardiogenic shock, severe dysrhythmia, re-MI, ventricular thrombus, angina)	1158	35	53	24	16
Martínez García, 2021, Cuba	2013 to 2020	PCS	Spanish	507	68± 11.7	347	24	ST-elevated MI	In-hospital MCC (cardiac arrest, HF, cardiogenic shock, severe dysrhythmia, re-MI, ventricular thrombus, angina)	1188	160	130	149	68

Table 1: Characteristics of included articles

Study	Data	Study design	Language	Sample size	Mean age	Male (n)	Timing of LGI (hrs)	Patients setting	Outcome	Cut off of LGI	TP	TN	FP	FN
Martínez Saldaña, 2018, Mexico	2016 to 2017	Cross	Spanish	34	59.7± 13.2	29	0	ST- and non-ST-elevated MI	3-day mortality	1601	4	10	16	4
Padilla-Cueto, 2019, Cuba	2011 to 2015	Cross	English	344	68 (58-76)	226	0	ST-elevated MI	One-year mortality	2200	44	219	37	44
Qi, 2022, China	214 to 2019	PCS	English	1256	67 (53 to 78)	930	0	ST- and non-ST-elevated MI	In-hospital mortality	1402	51	590	263	26
									In-hospital mortality	3593	15	256	42	13
Quiroga Castro-a, 2010, Argentina	2006 to 2007	PCS	Spanish	101	60	85	0	ST-elevated MI	In-hospital MCC (Cardiac death and HF)	1600	25	50	16	10
Quiroga Castro-b, 2010, Argentina	2007 to 2009	Cross	English	155	NR	NR	0	ST-elevated MI	In-hospital MCC (Cardiac death and HF)	1600	26	73	46	10
Rodríguez Jiménez, 2019, Cuba	2012 to 2015	PCS	Spanish	424	67.8±14.2	271	4	ST-elevated MI	In-hospital mortality	2122	44	220	147	13

Cross: Cross-sectional; FN: False negative; FP: False positive; HF: Heart failure; LGI: Leuko-glycemic index; MCC: Major cardiac complications; MI: Myocardial infarction; PCS: Prospective cohort study; RCS: Retrospective cohort study ST: ST segment; TN: True negative; TP: True positive

Table 2: Risk of bias assessment of included studies

Author	Risk of bias				Applicability			Overall
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard	
Cuesta-Mero, 2021	Low	Low	Low	Low	Low	Low	Low	Low risk
Diaz Benitez, 2016	Low	Low	Unclear	Low	Low	Low	Unclear	Some concern
Hirschson Prado, 2014	Low	Low	Low	Low	Low	Low	Low	Low risk
Leon-Aliz; 2014	Unclear	Low	Low	Low	Low	Low	Low	Low risk
Martínez García, 2021	Low	Low	Low	Low	Low	Low	Low	Low risk
Martínez Saldaña, 2018	Unclear	Low	Unclear	Low	Low	Low	Low	Some concern
Padilla-Cueto, 2019	Unclear	Low	Low	Low	Low	Low	Low	Low risk
Qi, 2022, China	Low	Low	Low	Low	Low	Low	Low	Low risk
Quiroga Castro-a, 2010	Low	Low	Low	Low	Low	Low	Low	Low risk
Quiroga Castro-b, 2010	Low	Low	Low	Unclear	Low	Low	Low	Low risk
Rodríguez Jiménez, 2019	Low	Low	Low	Low	Low	Low	Low	Low risk

2.5. Outcomes

The sought outcomes were mortality and major cardiac complications following acute MI. The definition of major cardiac complications varied upon studies and included cardiac arrest, cardiac death, heart failure, cardiogenic shock, severe dysrhythmia, re-MI, ventricular thrombus, and angina.

2.6. Risk of bias assessment

Since all the included studies were observational and our aim was to investigate the prognostic value of the LGI using sensitivity and specificity, the risk of bias was assessed using the QUADAS-2 tool (20). Two reviewers independently evaluated the studies based on the items provided in the QUADAS-2 questionnaire and scored them as low, high, or unclear on each item.

2.7. Level of evidence

The level of evidence was determined utilizing the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework (21). Through evaluation of the risk of bias, imprecision, inconsistency, indirectness, and publication bias as the items provided in the GRADE framework, the level of evidence was determined for each outcome.

2.8. Statistical Analysis

The extracted data were analyzed in STATA 14.0 statistical program (Stata Corp, College Station, TX, USA). The entered data in TP, TN, FP, and FN format were analyzed using the "midas" command. All analyses were outcome-based. The prognostic value of the LGI in predicting mortality and major cardiac complications was evaluated by reporting the sensitivity, specificity, positive and negative likelihood ratio, and prognostic odds ratio with a 95% confidence interval. To assess the heterogeneity among included studies, the I2 statistic and Q-test were used. Publication bias was evaluated using Deek's funnel plot test. Ultimately, the Fagan plot diagram was depictured for the LGI in predicting mortality and major cardiac complications to assess the post-test probability and its clinical importance. We estimated pre-test probability based on pooled prevalence of mortality or major cardiac complication among included studies.

3. Results

3.1. Article selection

A systematic search in four databases yielded 1073 non-duplicated records. Following the primary screening of title and abstracts, 30 full-text articles were retrieved. In the second step, 19 articles were excluded, and the remaining 11 were selected as eligible for the meta-analysis (15, 16, 19, 22-28). Moreover, in a manual search, 13 potentially relevant manuscript were found. All these 13 papers were theses and did not provide sufficient data. For example, some of the 13 theses had not reported data on acute MI, not measured the primary endpoints, and not reported the required data concerning our study aims. The reasons for excluding articles are provided in figure 1.

3.2. Summary of included studies

Among 11 eligible studies, there were 6 prospective and 1 retrospective cohort studies, along with 4 cross-sectional studies. There were 7 studies in Spanish, and the remaining 4 were published in English. These studies included 3701 patients suffering from acute MI. 72.1% of enrolled patients were male. The mean age of recruited patients ranged from 59.7 years to 68.2 years. In all included studies, the LGI measurement was performed within the first 24 hours following symptoms and prior to initiation of treatments. Mortality was reported in 9 studies, and the combination of major cardiac complications was present in 7 studies. The determined cut-offs for the LGI varied from 656.6 to 3593 among studies. Most of the studies reported a cut-off between 1000 to 2000. The characteristics of all eligible studies have been presented in Table 1.

3.3. Value of the LGI in prediction of mortality

Analysis showed that the area under the receiver operating characteristic (ROC) curve for the LGI in the prediction of mortality following acute MI was 0.77 (95% CI: 0.73 to 0.80), implicating the good value of this index (Figure 2). The sensitivity and specificity of the LGI in predicting mortality were 0.75 (95% CI: 0.62 to 0.84) and 0.66 (95% CI: 0.51 to 0.78), respectively (Supplementary figure 1).

Positive and negative likelihood ratios (positive LR and negative LR) and prognostic odds ratio were 2.20 (95% CI: 1.59 to 3.04), 0.38 (95% CI: 0.27 to 0.53), and 5.76 (95% CI: 3.60 to 9.22), respectively (Supplementary figure 2 and Figure 3).

Drawn Fagan plot, based on the assumption of pre-test probability of 11% for mortality derived from the studies, revealed that the LGI's positive and negative post-test probability were 21% and 5%, respectively (Figure 4).

3.4. Value of the LGI in the prediction of major cardiac complications

In this section, 10 studies were included in the analysis since one study reported all-cause mortality as outcome. Our Analyses demonstrated that the area under the ROC curve for the LGI in the prediction of major cardiac complications following acute MI was 0.81 (95% CI: 0.77 to 0.84), indicating an acceptable prognostic value for this index (Figure 2). The sensitivity and specificity of the LGI in predicting major cardiac complications were 0.84 (95% CI: 0.70 to 0.92) and 0.64 (95% CI: 0.49 to 0.84), respectively (Supplementary figure 3). Positive LR, Negative LR and prognostic odds ratio were 2.34 (95% CI: 2.21 to 3.34), 0.25 (95% CI: 0.13 to 0.45) and 9.52 (95% CI: 4.48 to 20.26), respectively (Supplementary figure 4 and Figure 5).

Drawn Fagan plot based on the assumption of pre-test probability of 38% for mortality derived from the studies indicated that the LGI's positive and negative post-test probability were 59% and 13%, respectively (Figure 4).

3.5. Risk of bias assessment

Quality assessment of included studies showed that 3 studies had unclear risk of bias regarding patient selection because of their retrospective nature. There was no clear definition of the reference standard in 2 studies, which made their status unclear in this item.

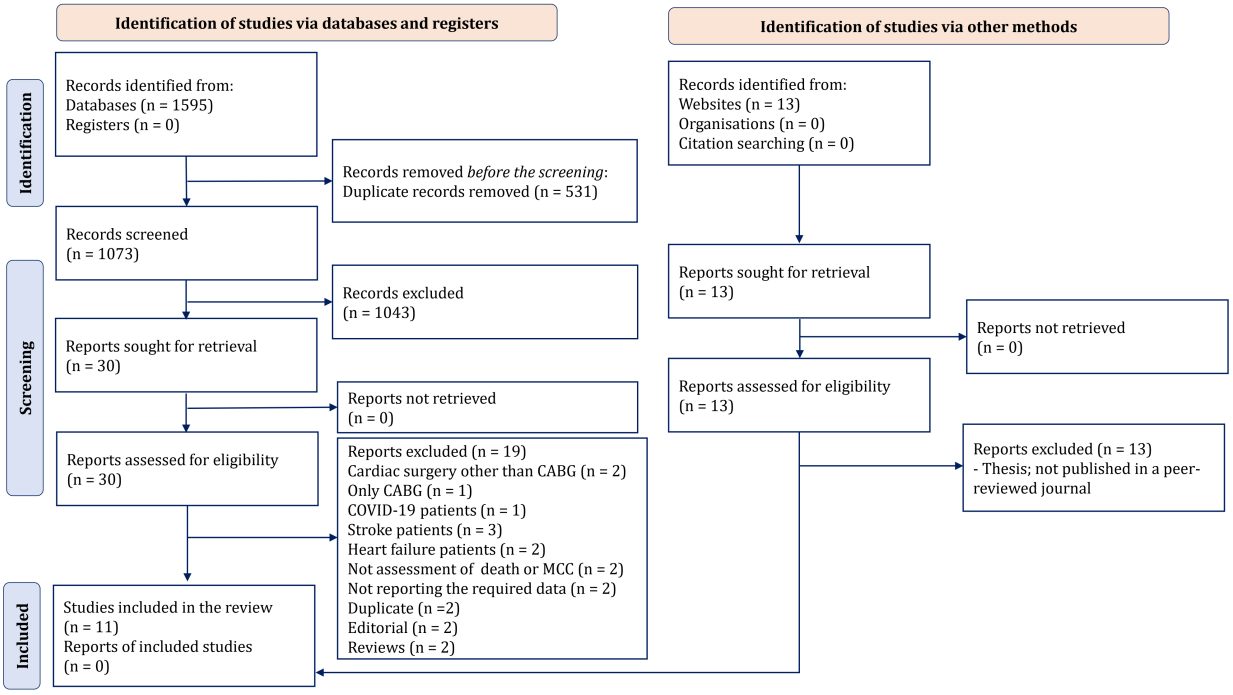

Figure 1: Flow diagram of the current study. CABG: Coronary artery bypass graft; MCC: Major cardiac complications.

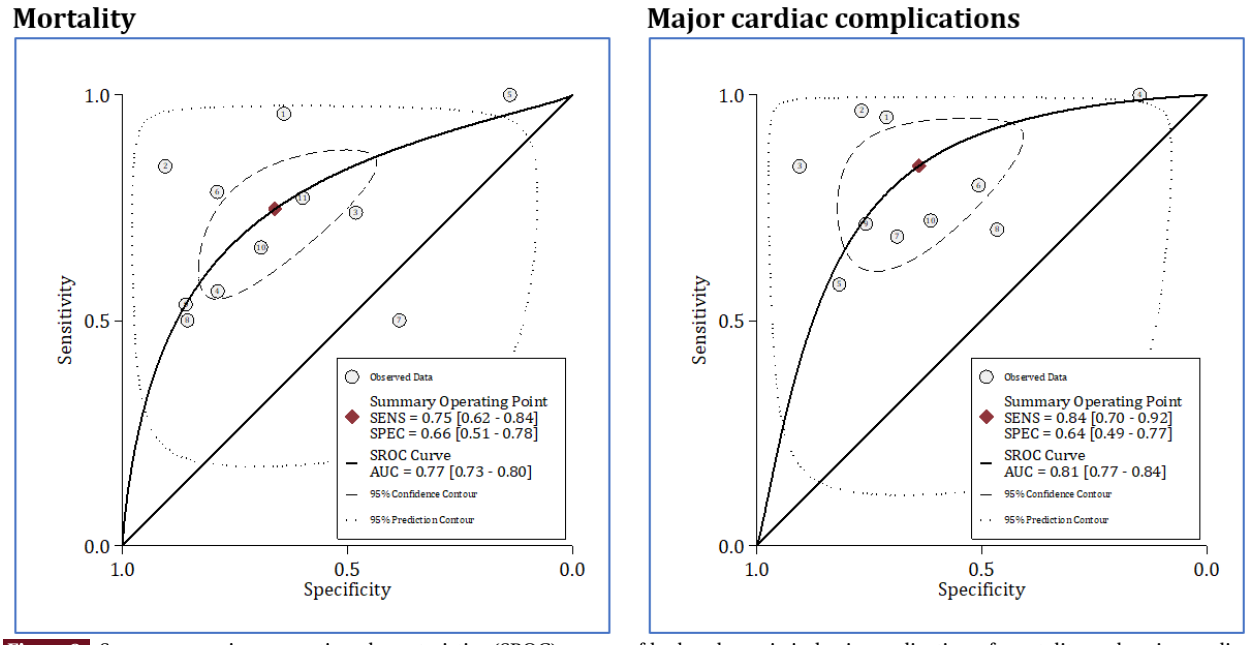

Figure 2: Summary receiver operating characteristics (SROC) curves of leuko-glycemic index in predication of mortality and major cardiac complications following acute myocardial infarction. AUC: area under the curve; SPEC: specificity; SENS: sensitivity.

Moreover, flow and timing could not be deduced from one study, causing it to be regarded as unclear. Finally, one study had not presented adequate data about the applicability of reference standards, which is thus considered unclear. In all remaining items, studies were low-risk. The overall risk of bias assessment was concluded as low in 9 studies and some concern in 2 studies (Table 2).

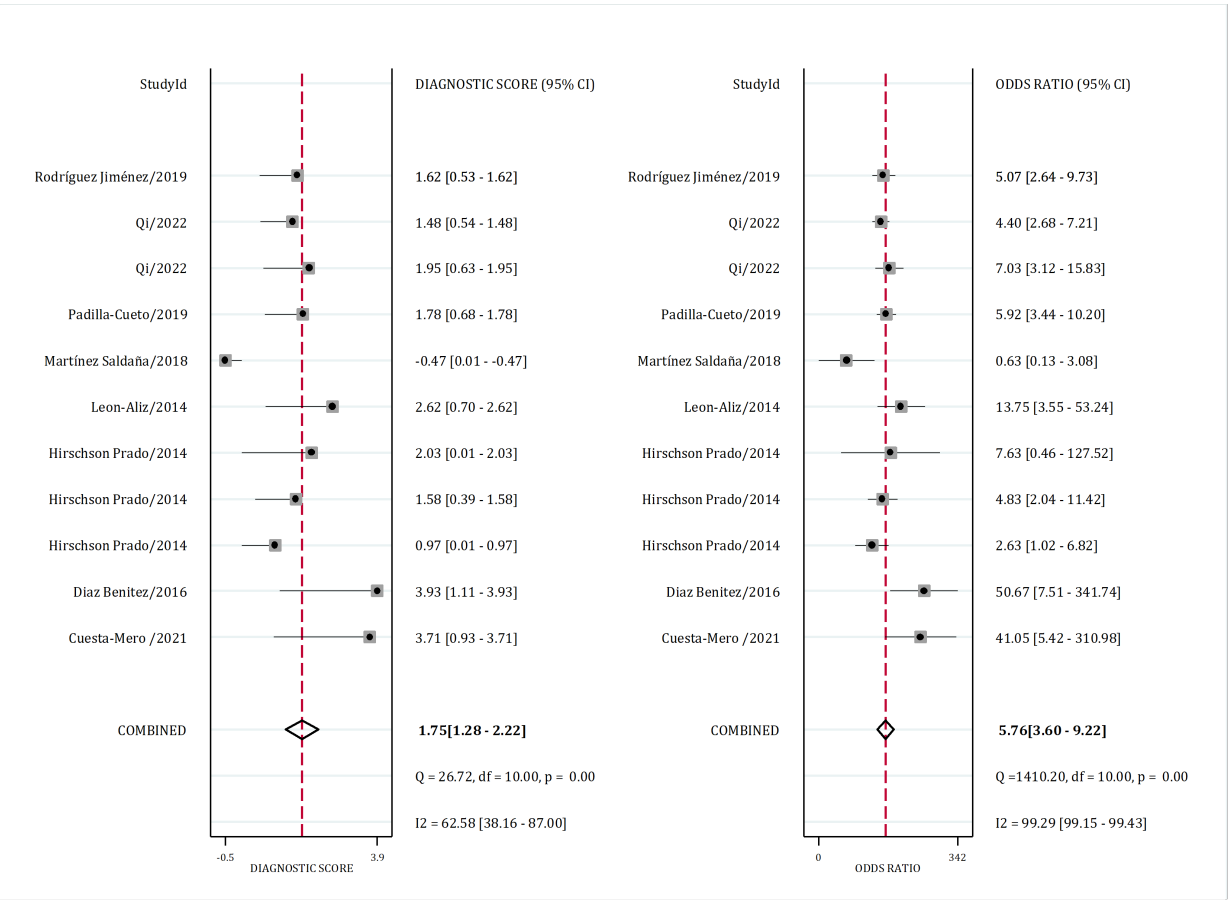

Figure 3: Odds ratio of leuko-glycemic index in predication of mortality following acute myocardial infarction. CI: confidence interval.

Table 3: Certainty of evidence based on GRADE framework

Outcome	Sample size	Prognostic odds ratio	Risk of bias	Imprecision	Inconsistency (I2)	Indirectness	Publication bias	Judgment and level of evidence
Mortality	3646	5.76 (95% CI: 3.60, 9.22)	Not serious	Not serious	Serious	Not serious	Not present	**Moderate:** Rated down 1 point • Presence of serious inconsistency Rated up 2 points • Very large magnitude of effect*
Major cardiac complications	2430	9.52 (95% CI: 4.48, 20.26)	Not serious	Not serious	Serious	Not serious	Likely	**Low:** Rated down 2 points • Presence of serious inconsistency • Possible publication bias Rated up 2 points • Very large magnitude of effect*

*, according to prognostic odds ratio. GRADE: Grading of Recommendations, Assessment, Development, and Evaluations; CI: confidence interval.

3.6. Publication bias

Deek's funnel plot revealed no publication bias among studies reporting the value of the LGI in predicting mortality following acute MI (p=0.48). However, there was evidence of publication bias in articles that surveyed major cardiac complications (p=0.03) (Supplementary figure 5).

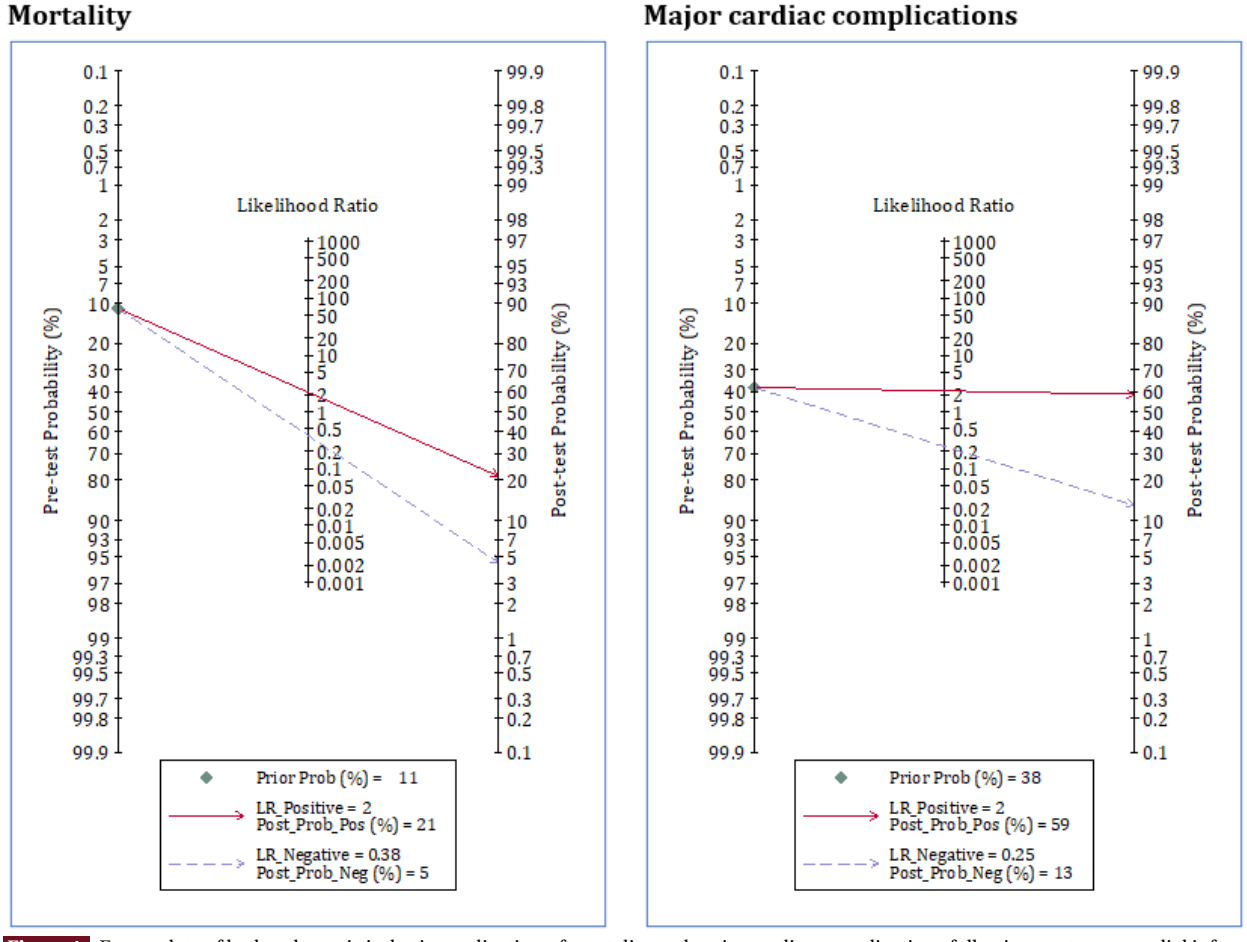

Figure 4: Fagan plots of leuko-glycemic index in predication of mortality and major cardiac complications following acute myocardial infarction. LR: Likelihood ratio; Prob: Probability; Post-Prob-Pos: Positive post-test probability; Post-Prob-Neg: Negative post-test probability.

3.7. Certainty of evidence

There was serious inconsistency in assessment of the prognostic value of LGI in prediction of mortality, while a very large magnitude of effect was observed (prognostic odds ratio=5.76). Therefore, level of evidence was graded as moderate.

Presence of serious inconsistency and possible publication bias rated down certainty of evidence two points in assessment of prognostic value of LGI in predicting major cardiac complication. However, a very large magnitude of effect was observed (prognostic odds ratio=9.52). Therefore, the level of evidence was deemed low (Table 3).

4. Discussion

Previous studies implicated a close link between admission hyperglycemia, regardless of diabetic status, and the short-term and long-term mortality among patients suffering from myocardial infarction (29, 30). Similarly, a greater leukocyte count on admission, which is representative of inflammation in the body, was associated with poor outcomes in ST segment elevation MI (STEMI) patients (31). With the backbone of mentioned findings, in 2010, Quiroga Castro et al. introduced the combination of two variables of blood glucose and leukocyte count as the leuko-glycemic index for predicting mortality and complications among MI patients (14). Since then, multiple studies have been conducted to survey the predictive value of the leuko-glycemic index. Hence, for the first time, we conducted a systematic review and meta-analysis to assess all studies available on this subject.

The present study demonstrated that the leuko-glycemic index has favorable sensitivity and accepted specificity in predicting in-hospital mortality among MI patients, irrespective of diabetes status. These results should be interpreted cautiously since the leuko-glycemic index is subject to limitations. Some studies demonstrated a difference in the predictive value of the leuko-glycemic index in diabetic and non-diabetic patients (15). Even though diabetes, per se, is as-

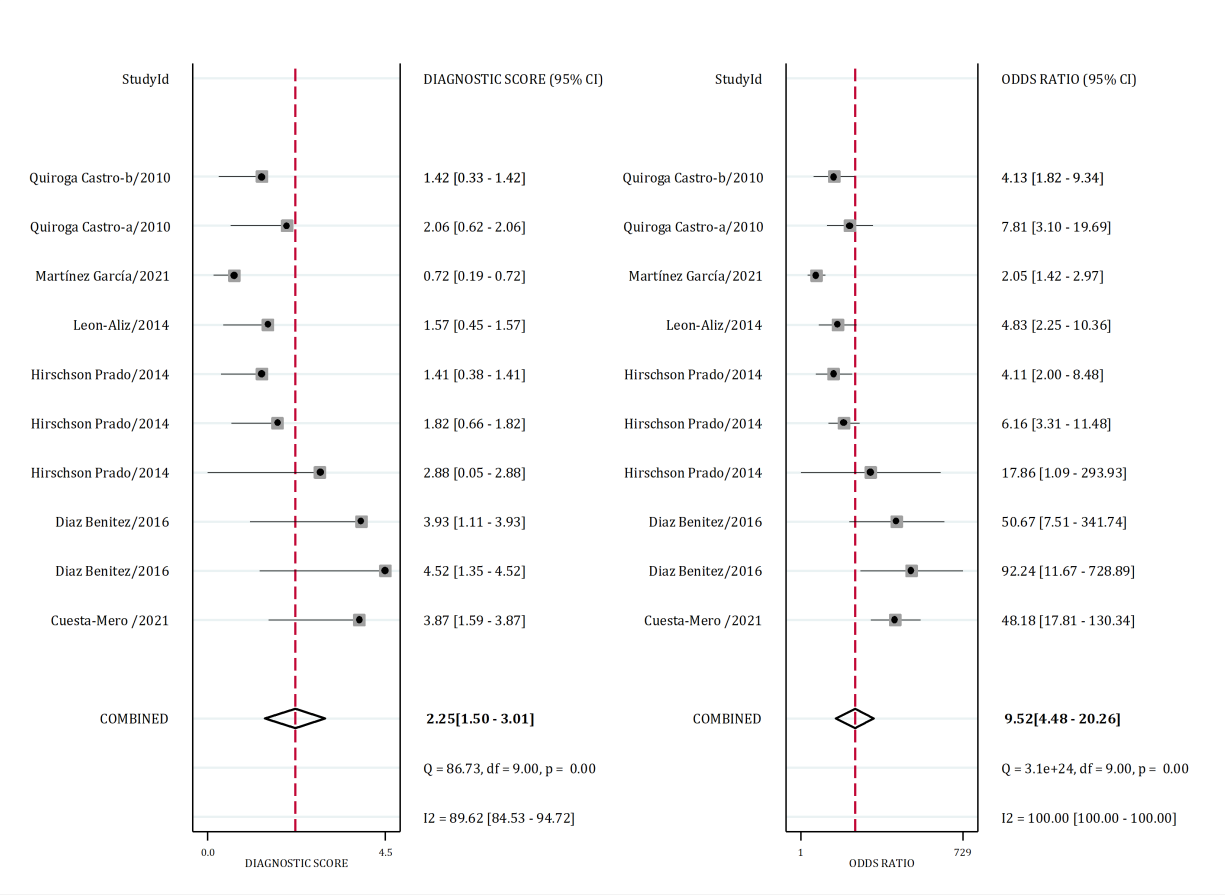

Figure 5: Odds ratio of leuko-glycemic index in predication of major cardiac complications following acute myocardial infarction. CI: confidence interval.

sociated with a higher burden of cardiovascular morbidity and mortality, it would be reasonable to use different cutoff points as baseline average blood glucose and its alteration in diabetic patients differ from nondiabetic patients. Nevertheless, the detrimental effect of hyperglycemia, regardless of diabetic status, persists even in response to treatment (32).

According to the estimated results, the LGI had 84% sensitivity and 64% specificity in predicting major cardiac complications in patients suffering from myocardial infarction. But based on the pre-test and post-test probability, the leuko-glycemic index does not significantly impact clinical decision-making. In a systematic review and meta-analysis, admission hyperglycemia was associated with a higher risk of overall arrhythmias, which is the cause of early complications following MI in diabetic and nondiabetic patients (35). Blood glucose levels and inflammatory markers are tethered together. Hyperglycemia is associated with higher concentrations of inflammatory cytokines that play a significant role in the secondary perpetuation of myocardial damage after MI (16, 19, 34). Inflammatory markers' increase after MI is linked to hypercoagulability, myocardial remodeling, and oxidative stress, culminating in adverse clinical events (35). We acknowledge the presence of limitations in our study. Primary endpoints of major cardiac complications and their follow-up periods varied among studies, and there was a lack of consensus. This heterogeneity in the definition of measured outcomes contributes to the wide range of reported cutoff points among referred studies.

The majority of studies included in the meta-analysis have a small sample size, with a maximum of 1256 patients in the most recent one. During our investigations, we found a sparsity of studies comparing the leuko-glycemic index with other prognostic indicators such as the TIMI, HEART, and GRACE scores. In addition, most of the studies found in the literature were conducted on the Hispanic/Latino populations, which raised concerns about geographical and ethnic bias. Further studies with robust methodology and racial diversity are warranted to address these limitations.

5. Conclusion

In the absence of advanced diagnostic modalities, the leuko-glycemic index could be an assistive tool for predicting in-hospital mortality of MI patients due to its availability, routine measurement, and low cost. However, the calculation of the leuko-glycemic index would not be clinically impressive regarding the major cardiac complications after MI. These conclusions are made on studies mainly investigating Latino/Hispanic populations, and their applicability to other populations is under question. Future studies are required to compare the other well-known predictive scores with the leuko-glycemic index.

6. Declarations

6.1. Acknowledgments

None.

6.2. Conflict of interest

The authors declare that there is no conflict of interest.

6.3. Fundings and supports

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6.4. Authors' contribution

Study design: AS, RS, SAF
Dara gathering: SAF, MV, SR
Analysis: SAF
Interpreting the results: AS, RS
Drafting: RS, SAF, SR
Critically revised: All authors
Read and approve final version: All authors

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Supplementary material 1: Full search syntax of the current study

PubMed

1- "Glycemic index"[MeSH Terms] OR ("leuko*"[All Fields] AND "glycemic"[Title/Abstract]) OR "leuko-glycemic"[Title/Abstract] OR "leuko-glycemic"[Title/Abstract] OR "Leukoglycemic"[Title/Abstract]

2- "Myocardial Ischemia"[MeSH Terms] OR "Acute Coronary Syndrome"[MeSH Terms] OR "Angina Pectoris"[MeSH Terms] OR "Angina, Stable"[MeSH Terms] OR "Angina, Unstable"[MeSH Terms] OR "Coronary Artery Disease"[MeSH Terms] OR "Coronary Occlusion"[MeSH Terms] OR "Coronary Stenosis"[MeSH Terms] OR "Coronary Thrombosis"[MeSH Terms] OR "Coronary Vasospasm"[MeSH Terms] OR "Myocardial Infarction"[MeSH Terms] OR "Anterior Wall Myocardial Infarction"[MeSH Terms] OR "Inferior Wall Myocardial Infarction"[MeSH Terms] OR "Non-ST Elevated Myocardial Infarction"[MeSH Terms] OR "ST Elevation Myocardial Infarction"[MeSH Terms] OR "Myocardial Reperfusion Injury"[MeSH Terms] OR "Myocardial Ischemia"[Title/Abstract] OR "Ischemic Heart Disease"[Title/Abstract] OR "Acute Coronary Syndrome"[Title/Abstract] OR "Unstable Angina"[Title/Abstract] OR "Angina Pectoris"[Title/Abstract] OR "Angina Pectori"[Title/Abstract] OR "Preinfarction Angina"[Title/Abstract] OR "Coronary Heart Disease"[Title/Abstract] OR "Coronary Artery Disease"[Title/Abstract] OR "Coronary Arteriosclerosis"[Title/Abstract] OR "Coronary Atherosclerosis"[Title/Abstract] OR "Coronary Occlusion"[Title/Abstract] OR "Coronary Stenosis"[Title/Abstract] OR "Coronary Thrombosis"[Title/Abstract] OR "Coronary Vasospasm"[Title/Abstract] OR "Myocardial Infarction"[Title/Abstract] OR "Myocardial Infarct"[Title/Abstract] OR "Heart Attack"[Title/Abstract] OR "Myocardial Reperfusion Injury"[Title/Abstract] OR "Myocardial Ischemic Reperfusion Injury"[Title/Abstract] OR "heart infarction"[Title/Abstract] OR "acute heart infarction"[Title/Abstract] OR "anterior myocardial infarction"[Title/Abstract] OR "Dressler syndrome"[Title/Abstract] OR "heart muscle necrosis"[Title/Abstract] OR "inferior myocardial infarction"[Title/Abstract] OR "MINOCA"[Title/Abstract] OR "non ST segment elevation myocardial infarction"[Title/Abstract] OR "posterior myocardial infarction"[Title/Abstract] OR "silent myocardial infarction"[Title/Abstract] OR "ST segment elevation myocardial infarction"[Title/Abstract] OR "acute coronary syndrome"[Title/Abstract] OR "non st segment elevation acute coronary syndrome"[Title/Abstract] OR "acute coronary syndrome"[Title/Abstract] OR "angina pectoris"[Title/Abstract] OR "cardiac allograft vasculopathy"[Title/Abstract] OR "coronary artery atherosclerosis"[Title/Abstract] OR "coronary artery constriction"[Title/Abstract] OR "coronary artery obstruction"[Title/Abstract] OR "coronary artery thrombosis"[Title/Abstract] OR "coronary subclavian steal syndrome"[Title/Abstract] OR "heart infarction"[Title/Abstract] OR "ischemic cardiomyopathy"[Title/Abstract] OR "Kounis syndrome"[Title/Abstract] OR "myocardial hibernation"[Title/Abstract] OR "no reflow phenomenon"[Title/Abstract] OR "silent myocardial ischemia"[Title/Abstract] OR "takotsubo cardiomyopathy"[Title/Abstract]

3- #1 AND #2

Embase

1- 'glycemic index'/exp OR 'leuko*glycemic':ab,ti OR 'leuko-glycemic':ab,ti OR 'leukoglycemic':ab,ti

2- 'heart infarction'/exp OR 'acute heart infarction'/exp OR 'anterior myocardial infarction'/exp OR 'Dressler syndrome'/exp OR 'heart atrium infarction'/exp OR 'heart infarction size'/exp OR 'heart muscle necrosis'/exp OR 'heart reinfarction'/exp OR 'heart ventricle infarction'/exp OR 'impending heart infarction'/exp OR 'inferior myocardial infarction'/exp OR 'MINOCA'/exp OR 'non ST segment elevation myocardial infarction'/exp OR 'posterior myocardial infarction'/exp OR 'silent myocardial infarction'/exp OR 'ST segment elevation myocardial infarction'/exp OR 'acute coronary syndrome'/exp OR 'non st segment elevation acute coronary syndrome'/exp OR 'acute coronary syndrome'/exp OR 'angina pectoris'/exp OR 'cardiac allograft vasculopathy'/exp OR 'coronary artery atherosclerosis'/exp OR 'coronary artery constriction'/exp OR 'coronary artery obstruction'/exp OR 'coronary artery thrombosis'/exp OR 'coronary subclavian steal syndrome'/exp OR 'heart infarction'/exp OR 'heart muscle ischemia'/exp OR 'ischemic cardiomyopathy'/exp OR 'Kounis syndrome'/exp OR 'myocardial hibernation'/exp OR 'no reflow phenomenon'/exp OR 'silent myocardial ischemia'/exp OR 'takotsubo cardiomyopathy'/exp OR 'Myocardial Ischemia':ab,ti OR 'Ischemic Heart Disease':ab,ti OR 'Acute Coronary Syndrome':ab,ti OR 'Unstable Angina':ab,ti OR 'Angina Pectoris':ab,ti OR 'Angina Pectori':ab,ti OR 'Preinfarction Angina':ab,ti OR 'Preinfarction Anginas':ab,ti OR 'Coronary Heart Disease':ab,ti OR 'Coronary Artery Disease':ab,ti OR 'Coronary Arteriosclerosis':ab,ti OR 'Coronary Atherosclerosis':ab,ti OR 'Coronary Occlusion':ab,ti OR 'Coronary Stenosis':ab,ti OR 'Coronary Thrombosis':ab,ti OR 'Coronary Vasospasm':ab,ti OR 'Myocardial Infarction':ab,ti OR 'Myocardial Infarct':ab,ti OR 'Heart Attack':ab,ti OR 'Myocardial Reperfusion Injury':ab,ti OR 'Myocardial Ischemic Reperfusion Injury':ab,ti OR 'heart infarction':ab,ti OR 'acute heart infarction':ab,ti OR 'anterior myocardial infarction':ab,ti OR 'Dressler syndrome':ab,ti OR 'heart atrium infarction':ab,ti OR 'heart infarction size':ab,ti OR 'heart muscle necrosis':ab,ti OR 'heart reinfarction':ab,ti OR 'heart ventricle infarction':ab,ti OR 'impending heart infarction':ab,ti OR 'inferior myocardial infarction':ab,ti OR 'MINOCA':ab,ti OR 'non ST segment elevation myocardial infarction':ab,ti OR 'posterior myocardial infarction':ab,ti OR 'silent myocardial infarction':ab,ti OR 'ST segment elevation myocardial infarction':ab,ti OR 'acute coronary syndrome':ab,ti OR 'non st segment elevation acute coronary syndrome':ab,ti OR 'acute coronary syndrome':ab,ti OR 'angina pectoris':ab,ti OR 'cardiac allograft vasculopathy':ab,ti OR 'coronary artery atherosclerosis':ab,ti OR 'coronary artery constriction':ab,ti OR 'coronary artery obstruction':ab,ti OR 'coronary artery thrombosis':ab,ti OR 'coronary subclavian steal syndrome':ab,ti OR 'heart infarction':ab,ti OR 'heart muscle ischemia':ab,ti OR 'ischemic cardiomyopathy':ab,ti OR 'Kounis syndrome':ab,ti OR 'myocardial hibernation':ab,ti OR 'no reflow phenomenon':ab,ti OR 'silent myocardial ischemia':ab,ti OR 'takotsubo cardiomyopathy':ab,ti

3- #1 AND #2

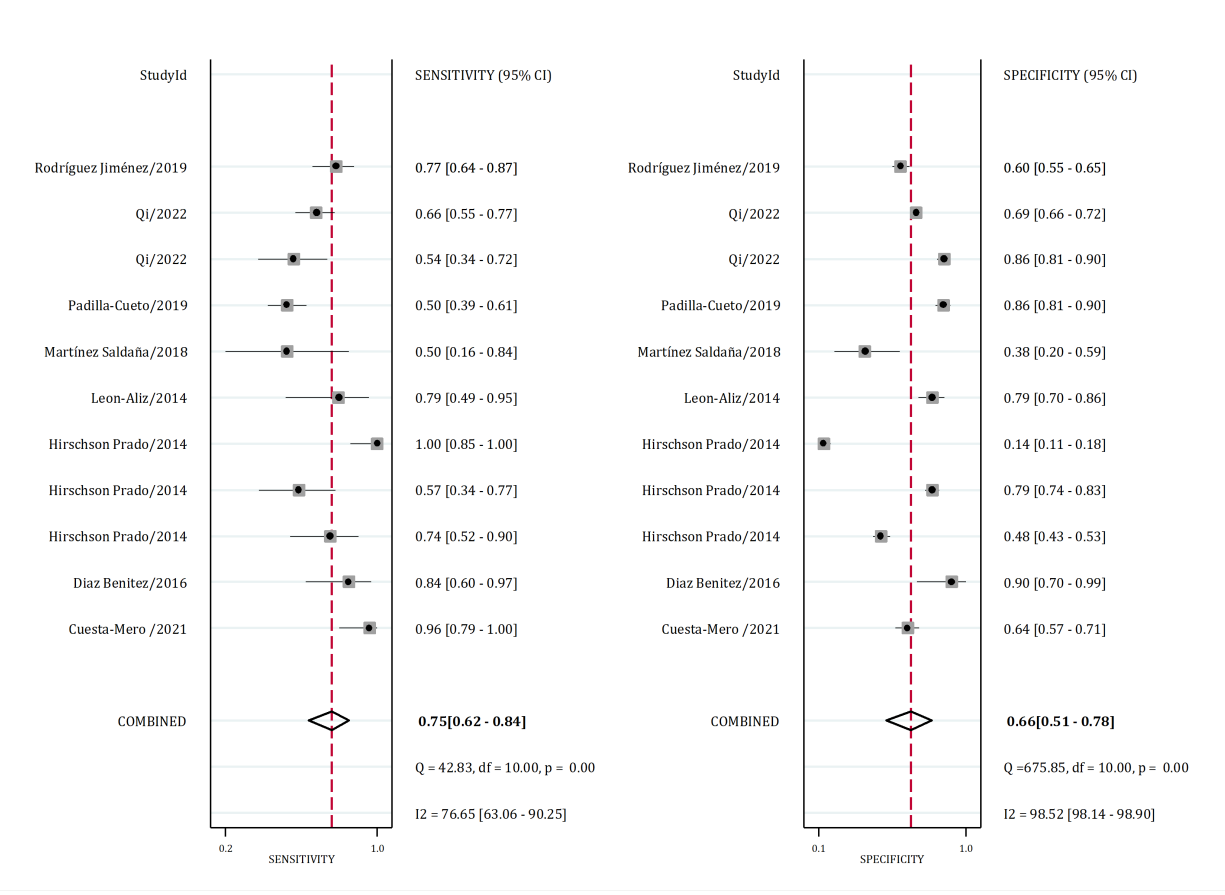
Scopus

1- TITLE-ABS-KEY("glycemic index" OR "leuko*glycemic" OR "leuko-glycemic" OR "leukoglycemic")

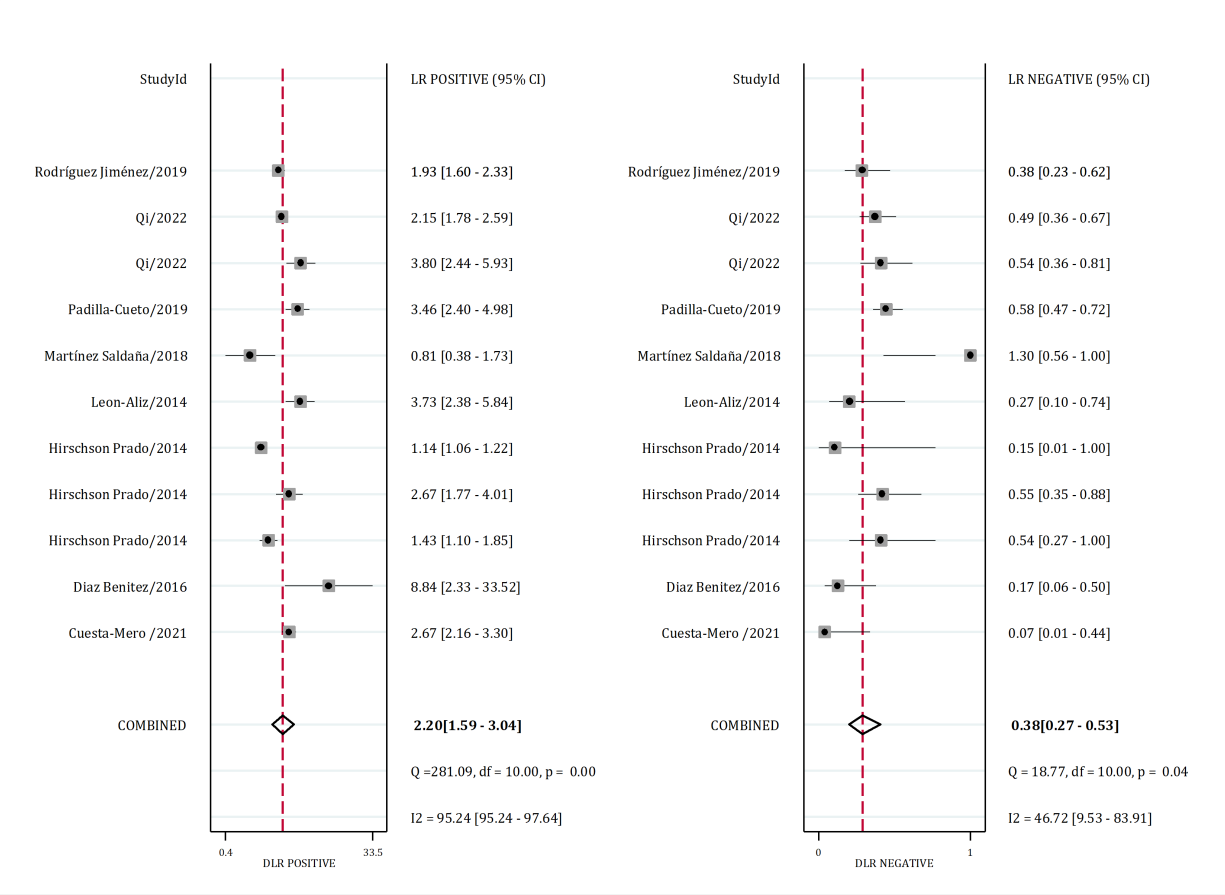
2- TITLE-ABS-KEY("Myocardial Ischemia" OR "Ischemic Heart Disease" OR "Acute Coronary Syndrome" OR "Unstable Angina" OR "Angina Pectoris" OR "Angina Pectori" OR "Preinfarction Angina" OR "Preinfarction Anginas" OR "Coronary Heart Disease" OR "Coronary Artery Disease" OR "Coronary Arteriosclerosis" OR "Coronary Atherosclerosis" OR "Coronary Occlusion" OR "Coronary Stenosis" OR "Coronary Thrombosis" OR "Coronary Vasospasm" OR "Myocardial Infarction" OR "Myocardial Infarct" OR "Heart Attack" OR "Myocardial Reperfusion Injury" OR "Myocardial Ischemic Reperfusion Injury" OR "heart infarction" OR "acute heart infarction" OR "anterior myocardial infarction" OR "Dressler syndrome" OR "heart atrium infarction" OR "heart infarction size" OR "heart muscle necrosis" OR "heart reinfarction" OR "heart ventricle infarction" OR "impending heart infarction" OR "inferior myocardial infarction" OR "MINOCA" OR "non

Supplementary material 1: Full search syntax of the current study

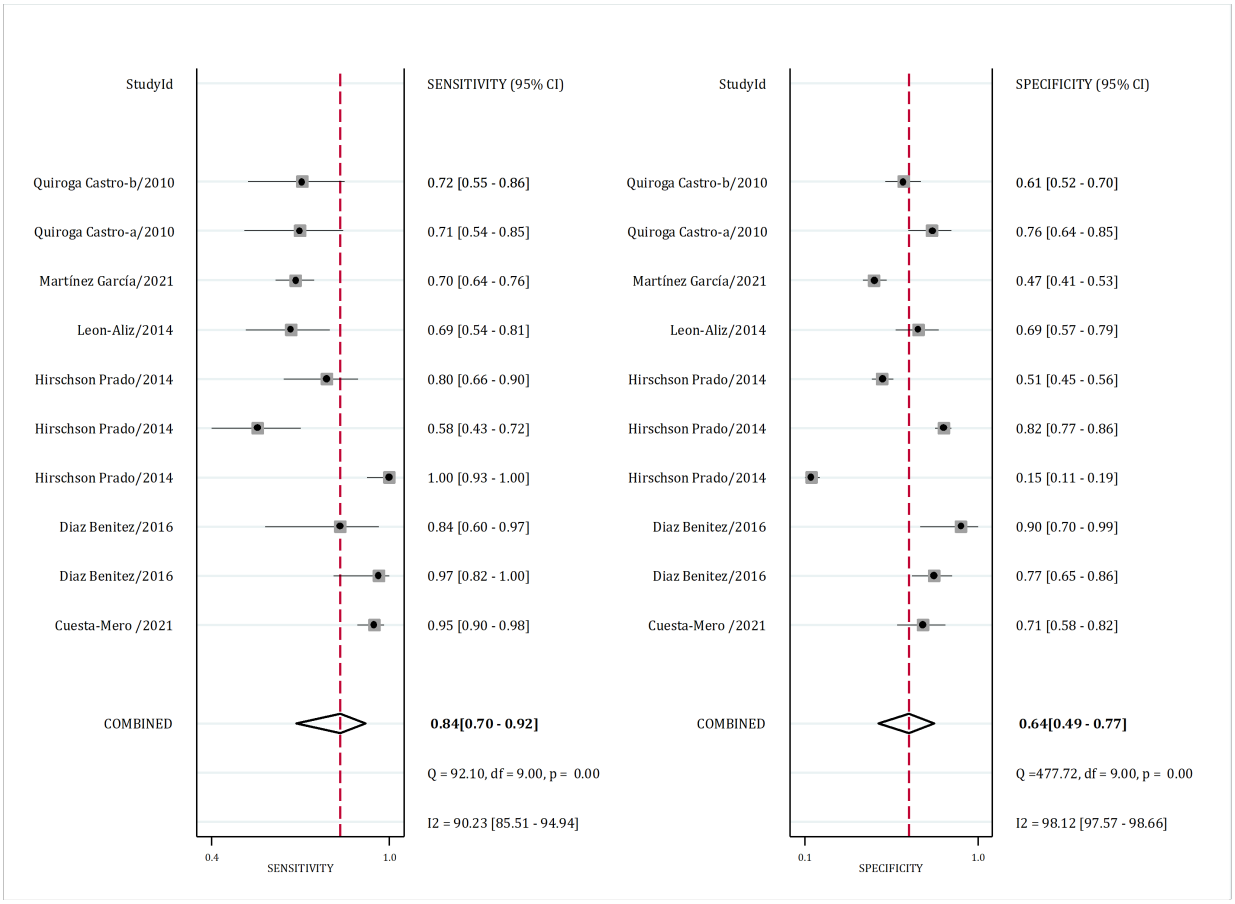
ST segment elevation myocardial infarction" OR "posterior myocardial infarction" OR "silent myocardial infarction" OR "ST segment elevation myocardial infarction" OR "acute coronary syndrome" OR "non st segment elevation acute coronary syndrome" OR "acute coronary syndrome" OR "angina pectoris" OR "cardiac allograft vasculopathy" OR "coronary artery atherosclerosis" OR "coronary artery constriction" OR "coronary artery obstruction" OR "coronary artery thrombosis" OR "coronary subclavian steal syndrome" OR "heart infarction" OR "heart muscle ischemia" OR "ischemic cardiomyopathy" OR "Kounis syndrome" OR "myocardial hibernation" OR "no reflow phenomenon" OR "silent myocardial ischemia" OR "takotsubo cardiomyopathy") 3- #1 AND #2
Web of Science (TS=("glycemic index" OR "leuko*glycemic" OR "leuko-glycemic" OR "leukoglycemic")) AND TS=("Myocardial Ischemia" OR "Ischemic Heart Disease" OR "Acute Coronary Syndrome" OR "Unstable Angina" OR "Angina Pectoris" OR "Angina Pectori" OR "Preinfarction Angina" OR "Preinfarction Anginas" OR "Coronary Heart Disease" OR "Coronary Artery Disease" OR "Coronary Arteriosclerosis" OR "Coronary Atherosclerosis" OR "Coronary Occlusion" OR "Coronary Stenosis" OR "Coronary Thrombosis" OR "Coronary Vasospasm" OR "Myocardial Infarction" OR "Myocardial Infarct" OR "Heart Attack" OR "Myocardial Reperfusion Injury" OR "Myocardial Ischemic Reperfusion Injury" OR "heart infarction" OR "acute heart infarction" OR "anterior myocardial infarction" OR "Dressler syndrome" OR "heart atrium infarction" OR "heart infarction size" OR "heart muscle necrosis" OR "heart reinfarction" OR "heart ventricle infarction" OR "impending heart infarction" OR "inferior myocardial infarction" OR "MINOCA" OR "non ST segment elevation myocardial infarction" OR "posterior myocardial infarction" OR "silent myocardial infarction" OR "ST segment elevation myocardial infarction" OR "acute coronary syndrome" OR "non st segment elevation acute coronary syndrome" OR "acute coronary syndrome" OR "angina pectoris" OR "cardiac allograft vasculopathy" OR "coronary artery atherosclerosis" OR "coronary artery constriction" OR "coronary artery obstruction" OR "coronary artery thrombosis" OR "coronary subclavian steal syndrome" OR "heart infarction" OR "heart muscle ischemia" OR "ischemic cardiomyopathy" OR "Kounis syndrome" OR "myocardial hibernation" OR "no reflow phenomenon" OR "silent myocardial ischemia" OR "takotsubo cardiomyopathy")



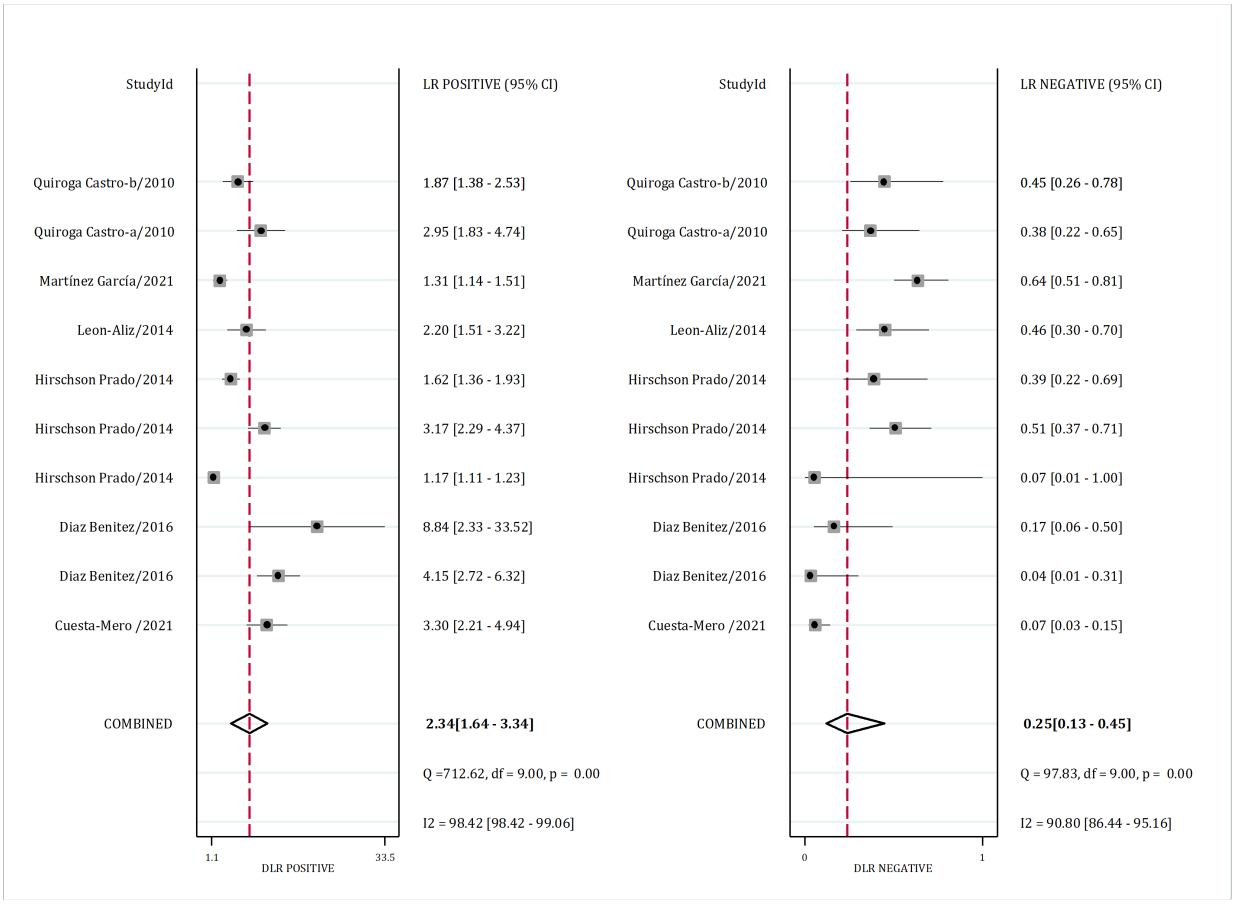
Supplementary figure 1: Sensitivity and specificity of leuko-glycemic index in predication of mortality following acute myocardial infarction. CI: confidence interval.



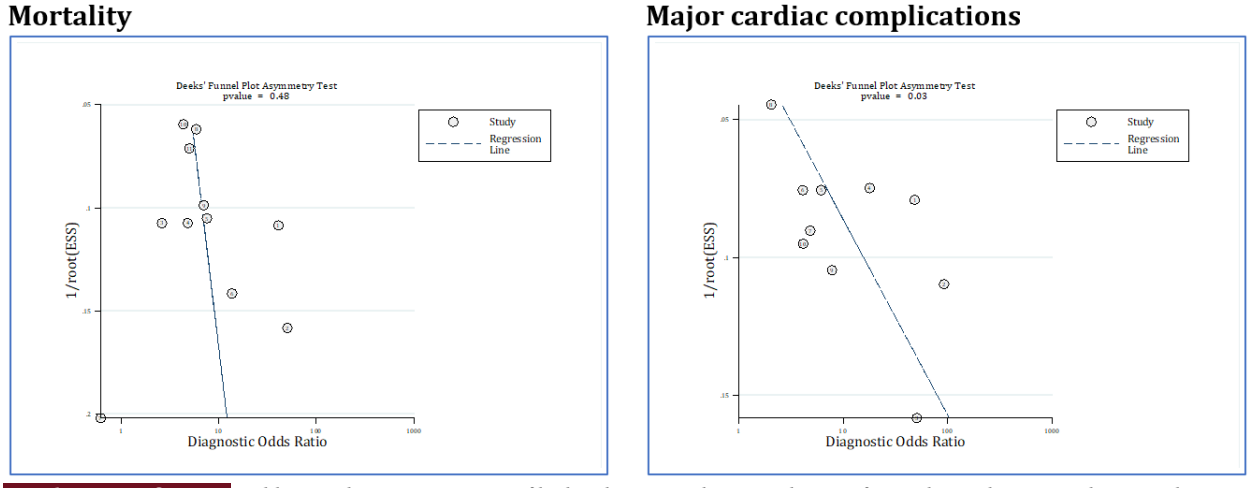
Supplementary figure 2: Positive and negative likelihood ratio (LR) of leuko-glycemic index in predication of mortality following acute myocardial infarction. CI: confidence interval.



Supplementary figure 3: Sensitivity and specificity of leuko-glycemic index in predication of major cardiac complications following acute myocardial infarction. CI: confidence interval.



Supplementary figure 4: Positive and negative likelihood ratio (LR) of leuko-glycemic index in predication of major cardiac complications following acute myocardial infarction. CI: confidence interval.



Supplementary figure 5: Publication bias in assessment of leuko-glycemic index in prediction of mortality and major cardiac complications following acute myocardial infarction.