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A systematic review of the role of systemic inflammation-based prognostic scores in patients with abdominal aortic aneurysm

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ABSTRACT

Background and aims: Activation of the systemic inflammatory response (SIR) is associated with inferior outcomes across a spectrum of disease. Routinely available measures of the SIR (neutrophil:lymphocyte ratio (NLR), platelet:lymphocyte ratio (PLR), systemic immune-inflammatory index (SII), systemic inflammatory grade (SIG)) have been shown to provide prognostic value in patients undergoing surgical intervention. The present study aimed to review the literature describing the prognostic association of NLR, PLR, SII and SIG in patients undergoing intervention for abdominal aortic aneurysm (AAA).

Methods: This PRISMA guidelines were followed. The MEDLINE database was interrogated for relevant studies investigating the effect of peri-operative systemic inflammation-based prognostic systems on all-cause mortality in patients undergoing OSR and EVAR for AAA. Inter-study heterogeneity precluded meaningful meta-analysis; qualitative analysis was instead performed.

Results: There were 9 studies included in the final review reporting outcomes on a total of 4571 patients; 1256 (27 %) patients underwent OSR, and 3315 (73 %) patients underwent EVAR. 4356 (95 %) patients underwent a procedure for unruptured AAA, 215 (5 %) patients underwent an emergency procedure for ruptured AAA0.5 studies reported early (inpatient or 30-day) mortality; 2 of these found that elevated NLR predicted inferior survival, however PLR did not provide prognostic value. 6 studies reported long-term mortality; elevated NLR (5 studies), PLR (1 study), and SIG (1 study) predicted inferior survival.

Conclusions: It appears that activation of the SIR is associated with inferior prognosis in patients undergoing intervention for AAA, however the evidence is limited by heterogenous methodology and lack of consensus regarding optimal cutoff.

Prospero database registration number: CRD42022363765.

1. Introduction

Activation of the systemic inflammatory response (SIR) is commonly observed in multiple chronic illnesses [1]. Additionally, we recently reported on the association between the SIR and outcomes in patients with lower extremity arterial disease [2]. Atherosclerosis has emerged as a pathology largely driven by inflammation [3], and an association between chronic inflammation and increased risk of long-term cardiovascular mortality has been described [4]. Activation of the SIR appears to influence prognosis in patients with a range of pathologies [5–7], and is a potential target for therapeutic modulation to improve outcomes. Prognostication using systemic inflammation-based scoring systems is currently limited to the research setting, however several scoring systems show promise in their potential application to the clinical setting.

Abdominal aortic aneurysm (AAA) is a condition defined as pathological dilatation of the aorta to greater than 50 % above its normal diameter. The prevalence increases with age, and may be as high as 4 % in males over 65[8]. Though not a conventional consequence of occlusive atherosclerotic disease, AAA shares similar risk factors with atherosclerosis and synchronous atherosclerotic and aneurysmal disease is not uncommon [9]. Repair of unruptured AAA (uAAA) is intended to prevent future rupture (rAAA), and is indicated once AAA diameter reaches 55 mm, with contemporary evidence suggesting no benefit to repair below this size [10]. rAAA is a terminal event without intervention, and carries a 40–50 % mortality in patients surviving to reach hospital [9].

Repair strategies for AAA consist of open surgical repair (OSR) or endovascular aneurysm repair (EVAR). To perform OSR a midline

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laparotomy is performed, the aneurysm sac is opened, and a prosthetic interposition graft is sutured to replace the diseased aorta. To perform EVAR a modular stent-graft system within the aneurysm is delivered, thereby excluding the aneurysm sac from the circulation and ameliorating the risk of rupture. Infrarenal AAA can be treated by standard EVAR; more complex AAA which may involve the ostia of the visceral vessels can be treated by fenestrated and branched endografts (F/B-EVAR).

The neutrophil:lymphocyte and platelet:lymphocyte ratios (NLR, PLR) are markers of the SIR derived from the absolute neutrophil, platelet, and lymphocyte counts on the full blood count. With regards to NLR, varying thresholds exist to define the pathological state, with <3.0, 3.0–5.0, and >5.0 being the most widely reported [6]. Thresholds of PLR are less well described. Increased NLR and PLR have been reported to predict inferior post-operative outcome in a range of conditions [6,7,11–16], with a more extensive evidence base supporting the prognostic role of NLR than that of PLR.

The systemic immune-inflammatory index (SII) is an alternative prognostic score originally described in patients with hepatocellular carcinoma [17]. Based on the full blood count, it is calculated by: platelet count x (neutrophil count/lymphocyte count). A diagnostic threshold of 330 has been proposed by the original authors though this lacks external validation.

The modified Glasgow Prognostic Score (mGPS) is a prognostic scoring system based on the acute phase protein response [18], calculated using absolute values of CRP (<10 mg/L) and albumin (<35 g/L). Originally derived from patients with cancer, the prognostic value of mGPS has subsequently been reported in several cancer and non-cancer conditions [7,19,20]. NLR and mGPS have been combined into the composite Systemic Inflammatory Grade (SIG), aiming to provide a more comprehensive measure both the acute-phase and differential white cell responses [5]. SIG appears to be associated with prognosis in patients undergoing curative treatment for colorectal cancer [5].

This review aims to summarise the contemporary evidence base describing the association between systemic inflammation-based prognostic scoring systems in predicting mortality in patients undergoing intervention for AAA.

2. Materials & methods

This review and search strategy was carried out in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Following preliminary literature search, there was a clear lack of prospective data available, therefore both prospective and retrospective studies were included. Furthermore, there was a clear lack of evidence reporting outcomes relating to mGPS in the eligible patient group. This lead to NLR, PLR, SII and SIG being chosen as the variables of interest. No ethical approval was required as individual patient data were not accessed. The review protocol was registered with the PROSPERO database (Registration Number: CRD42022363765).

2.1. Outcomes

The primary outcome of interest was the overall survival following intervention for AAA (either endovascular or open surgical repair, elective or emergency) in patients subgrouped by periprocedural NLR, PLR, SII, or SIG reported as categorical or continuous variables. The secondary outcome was how each study defined “high” and “low/normal” NLR PLR, or SII (SIG is already defined as a categorical variable, therefore was not included in these analyses).

2.2. Search strategy

The MEDLINE database was accessed electronically using the PubMed (National Centre for Biotechnology Information, U.S. National Library of Medicine, Bethesda MD, USA) search engine. The SCOPUS database (Elsevier, Amsterdam, Netherlands) was also accessed electronically. The search was conducted on the February 14, 2024; any papers published after this date are not included in this review. Though NLR was first described in 1967 [21] the first widespread clinically relevant studies reporting NLR, PLR, SII, and SIG were published in 2001, 2010, 2014 and 2021 respectively [5,17,22,23], therefore studies published before 2001 were excluded. Review articles, case reports, editorials/comments, animal studies, and studies unavailable in English as a full text version were excluded. The following search string was used:

“((NLR) OR (PLR) OR (SII) OR (SIG)) AND ((EVAR) OR (AAA) OR (aneurysm))”

This search term was applied to study title, key words, and Medical Subject Heading (MeSH) terms. Duplicate results were screened and the duplicate record removed from full paper screening. Relevant review articles underwent bibliography screening to identify additional relevant papers. Abstract screening was performed on the initial results to generate a list of studies to undergo full paper screening for final inclusion.

2.3. Data extraction

Data extracted from study documents include.

- Study design (centres, follow-up, prospective/retrospective) and study information (journal, authors, year).
- Baseline clinical and demographic data of patients.
- Classification of "high" vs. "low/normal" i.e. cut-off of NLR/PLR/SII (whether using data derived cut-offs or absolute values), or whether analysed as a continuous variable.
- Survival data for overall survival, where hazard ratio and 95 % confidence intervals are reported these were extracted. Where univariate and multivariate results are reported, relevant multivariate values were preferred for inclusion in this review.

The risk of bias in each study was assessed using the Cochrane Quality in Prognostic Studies (QUIPS) tool to systematically assess and record bias [24].

Preliminary literature review showed that significant heterogeneity between outcome measures reported and patient selection across all studies precluded meaningful meta-analysis. Therefore, studies were grouped based on their reporting of NLR, PLR SII and/or SIG in relation to outcomes in patients undergoing OSR and/or EVAR. Qualitative review of each of these subgroups was performed.

3. Results

The study selection process is summarised in the PRISMA diagram in Fig. 1. There were 9 studies included in the final review reporting outcomes on a total of 4571 patients [25–32]; 1256 (27 %) patients underwent OSR, and 3315 (73 %) patients underwent EVAR. 4356 (95 %) patients underwent a procedure for uAAA, 215 (5 %) patients underwent an emergency procedure for rAAA.

The variable of interest was NLR in 5 studies, PLR in 1 study, both NLR & PLR in 2 studies, with 1 study reporting SII and 1 study reporting SIG. The characteristics of each study and main outcomes are summarised in Table 1. Values of NLR or PLR were derived from pre-operative blood results in 7 studies, and from post-operative blood results in 1 study. The studies reporting SII and SIG reported values based on pre-operative blood results. All studies were retrospective, and 7 were single centre whilst 1 (Bath et al. 2019 [30]) was based on registry data from multiple centres and 1 (Bradley et al. 2023 [33]) was multicentre. Table 2 summarises the results of each study’s primary outcome.

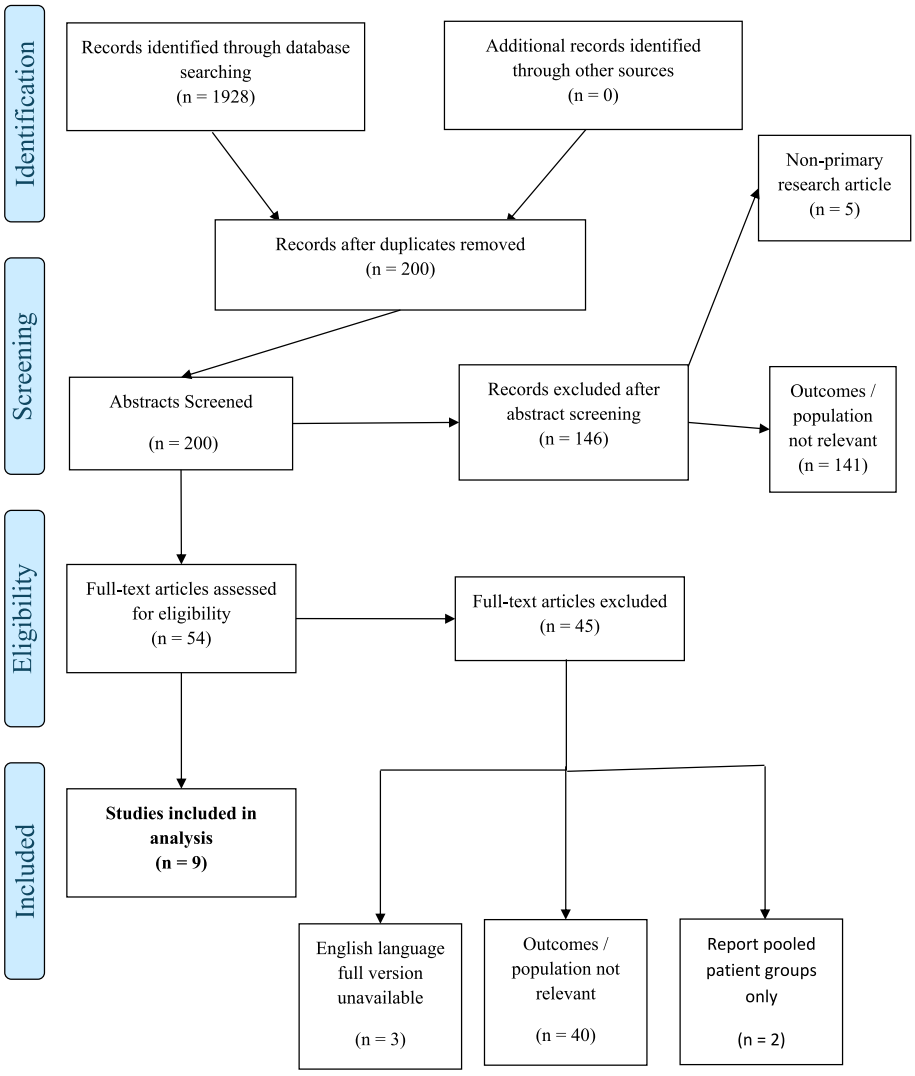

Fig. 1. PRISMA diagram showing study inclusion.

Table 1
Study design of the included studies investigating the effect of the SIR on mortality following OSR/EVAR for AAA.

Authors	Country	Design	Centres	Parameter	Pre/Post-Op	Procedure	Priority
Bradley et al. (2023) [33]	UK	Retrospective	Multicentre	SIG	Pre-op	506 EVAR	506 uAAA
Ko et al. (2021) [25]	S. Korea	Retrospective	Single	NLR, PLR	Pre-op	334 OSR	236 uAAA, 98 rAAA
Octeau et al. (2021) [26]	USA	Retrospective	Single	NLR	Pre-op	777 EVAR	765 uAAA, 12 rAAA
Lecumberri et al. (2021) [27]	Spain	Retrospective	Single	NLR, PLR, SII	Pre-op	284 EVAR	284 uAAA
King et al. (2020) [28]	USA	Retrospective	Single	NLR	Pre-op	108 EVAR	108 uAAA
Bath et al. (2019) [30]	USA	Retrospective	Multicentre Registry Data	NLR	Post-op	1529 EVAR, 379 OSR	1908 uAAA
Lareyre et al. (2019) [29]	France	Retrospective	Single	PLR	Pre-op	113 OSR, 111 EVAR	199 uAAA, 25 rAAA
Kordzadeh et al. (2015) [31]	UK	Retrospective	Single	NLR	Pre-op	80 OSR	80 r AAA
Appleton et al. (2014) [32]	UK	Retrospective	Single	NLR	Pre-op	350 OSR	350 uAAA
						1256 OSR, 3315 EVAR	**4356 uAAA, 215 rAAA**
						Total n = 4571	

3.1. Outcomes relating to NLR in patients undergoing OSR

5 studies reported outcomes by NLR on cohorts of patients undergoing OSR, with one of these (Bath et al. 2019 [30]) reporting on a combined OSR and EVAR cohort. 3 studies reported increased mortality associated with elevated NLR with follow-up ranging from 30 days to 1 year, whilst 2 studies did not observe a significant association.

Ko et al. (2021) [25] report 1-year mortality on a cohort of 334 patients with rAAA (n = 98) and uAAA (n = 236) undergoing OSR. NLR was analysed from preoperative blood sampling though the specific timing of this sample is not reported. In all patients, high NLR was associated with increased 1-year mortality on multivariate analysis (OR 1.09, 95 % CI 1.02–1.16, $p < 0.05$). In the rAAA subgroup, elevated NLR was associated with increased 1-year mortality on multivariate analysis (OR 1.14, 95 % CI 1.03–1.27, $p < 0.05$). NLR was not associated with survival in the uAAA subgroup.

Kordzadeh et al. (2015) [31] included 80 consecutive patients undergoing OSR for rAAA, with NLR calculated from pre-operative blood samples, without specific report of timing of sampling. NLR >5.0 was used to subgroup patients, with 25 patients in the "low NLR" subgroup

Table 2
Main findings of included studies investigating the effect of the SIR on mortality following OSR/EVAR for AAA.

Authors	Follow-Up	Primary Outcome	Summary of Results of Primary Outcome
Bradley et al. (2023) [33]	68.0 months (median)	Mortality during follow-up	**All patients:** Increasing SIG; HR 1.2, (95 % CI 1.02–1.40, $p < 0.05$).
Ko et al. (2021) [25]	12.0 months (final)	12.0-month mortality	**All patients:** NLR (Continuous); OR 1.09, (95 % CI 1.02–1.16), $p < 0.05$. PLR (Continuous); NS. **rAAA:** NLR (Continuous); OR 1.14, (95 % CI 1.03–1.27), $p < 0.05$. PLR (Continuous); OR 0.99, (95 % CI 0.98–0.99), $p < 0.05$. **uAAA:** NLR & PLR (Continuous); NS.
Octeau et al. (2021) [26]	48.0 months (median)	Mortality during follow-up	**All patients:** NLR (≥3.6); HR 1.59, (95 % CI 1.22–2.06), $p = 0.001$. NLR (Continuous); HR 1.05, (1.02–1.08), $p < 0.01$.
Lecumberri et al. (2021) [27]	60.0 months (final)	2-year and 5-year survival	**All patients, 2-year survival:** NLR (≥3.0); HR 1.98, (95 % CI 1.07–3.66), $p < 0.05$. PLR (Continuous); HR 1.002, $p < 0.05$. SII (Continuous); HR 1.000, $p = 0.066$. **All patients, 5-year survival:** NLR (≥3.0); HR 1.98, (95 % CI 1.07–3.66), $p < 0.05$. PLR (Continuous); HR 1.002, $p < 0.05$. SII (Continuous); HR 1.000, $p < 0.05$.
King et al. (2020) [28]	36.4 months (median)	Mortality during follow-up	**All patients:** NLR (≥4.0); HR 1.19, (95 % CI 1.12–1.27), $p < 0.001$
Bath et al. (2019) [30]	Inpatient (<30 days) (final)	Inpatient (<30 days) mortality	**All patients:** NLR; NS.
Lareyre et al. (2019) [29]	Inpatient (<30 days) (final)	Inpatient (<30 days) mortality	**All patients:** PLR; NS.
Kordzadeh et al. (2015) [31]	Inpatient (<30 days) (final)	Inpatient (<30 days) mortality	**All patients**: NLR; NS.
Appleton et al. (2014) [32]	NR (minimum 12 months)	Mortality during follow-up, 30-day mortality	**Overall Mortality:** NLR (≥5.0) 50.0 % mortality vs. NLR (<5.0) 34.2 % mortality, $p < 0.05$. **30-day Mortality:** NLR (≥5.0) 23.0 % mortality vs. NLR (<5.0) 6.7 % mortality, $p < 0.05$.

NS; not significant ($p > 0.05$).

and 55 patients in the "high NLR" subgroup. The 30-day mortality in low vs. high subgroups was 8.0 % vs. 16.4 % ($p = 0.488$). Regression analyses were not performed due to low absolute number of events.

Appleton et al. (2014) [32] recruited 350 consecutive patients undergoing elective OSR for uAAA. All patients were followed-up for a minimum of 12 months though median follow-up is not reported. 30-day mortality in the patients with high NLR was 23.0 % vs. 6.7 % in the low NLR group ($p < 0.01$). Each of the 30-day deaths in patients with high NLR were due to myocardial infarction. Overall mortality during the follow-up period was 50.0 % vs. 34.2 % in the high vs. low NLR groups ($p < 0.05$).

Bath et al. (2019) [30] performed retrospective registry interrogation of patients undergoing elective OSR (n = 379) and EVAR (n = 1529) for AAA. Due to the limitations of their methodology, only inpatient mortality is reported. NLR was recorded from post-operative results. Results are presented as a combined cohort of both procedure types. On multivariate analysis, OSR was associated with increased inpatient mortality (OR 11.8, 95 % CI 5.26–26.60, $p < 0.05$), but high NLR was not ($p > 0.05$).

3.2. Outcomes relating to NLR in patients undergoing EVAR

4 studies reported outcomes by NLR in cohorts of patients undergoing EVAR, with one of these (Bath et al. 2019 [30]) reporting on a combined OSR and EVAR cohort (reported previously). 3 studies reported increased mortality in patients with elevated NLR, whilst 1 study did not observe a significant association.

Octeau et al. (2021) [26] included 777 patients undergoing procedures over a 16-year period, who were followed up for a median of 4 years. NLR values were taken from pre-operative blood sampling within 6 months of surgery. A multivariate model including age, cardiac comorbidity, aneurysm diameter, intraoperative complications, diabetes as covariates found that NLR (High) (HR 1.59, 95 % CI 1.22–2.06, $p = 0.001$) and NLR (continuous) (HR 1.05, 95 % CI 1.02–1.08, $p = 0.003$) were predictive of mortality. This cohort of patients included 12 patients undergoing EVAR for rAAA; we note that emergency procedure was not included as a covariate in this multivariate model.

Lecumberri et al. (2021) [27] report on 284 patients undergoing elective EVAR with follow-up for 5 years in all patients. Their survival analysis included the development of a predictive regression model using significant covariates (haemoglobin, statin use, atrial fibrillation, heart failure, coronary artery disease) and assessing response of goodness of fit parameters when NLR or PLR were added to the model. NLR had significant univariate predictive value on 2- and 5-year survival (HR 1.07 and 1.07 respectively, $p < 0.05$ and $p < 0.01$). When added to the predictive model NLR increased the continuous net reclassification index ($p < 0.05$) however did not significantly increase model C-statistic. Subsequent analysis based on dichotomous NLR values revealed that NLR ≥3.0 was independently associated with inferior 2-year (HR 1.98, 95 % CI 1.07–3.66, $p < 0.05$) and 5-year (HR 1.84, 95 % CI 1.22–2.78, $p < 0.05$) survival.

King et al. (2020) [28] report on a cohort of 108 patients undergoing elective EVAR, with NLR values taken within 30 days prior to surgery. Median follow-up was 36.4 months. On multivariate analysis, High NLR was associated with mortality (HR 1.19, 95 % CI 1.12–1.27, $p < 0.001$).

3.3. Outcomes relating to PLR in patients undergoing OSR

2 studies reported outcomes by PLR in cohorts of patients undergoing OSR, with one of these studies (Lareyre et al. 2019) [29] reporting on a combined OSR and EVAR cohort. 1 study observed reduced mortality associated with elevated PLR, and 1 study did not observe a significant association.

Ko et al. (2021, described in the previous section) [25] also reported outcomes on pre-operative PLR. In all patients, PLR was not significantly associated with survival, nor was it associated in the uAAA subgroup. In the rAAA subgroup, elevated PLR was associated with reduced 1-year mortality on multivariate analysis (OR 0.99, 95 % CI 0.98–0.99, $p < 0.05$).

Lareyre et al. (2019) [29] investigated the effect of pre-operative PLR on 30-day mortality in a combined cohort of patients with rAAA and uAAA undergoing either OSR or EVAR. Outcomes in open and endovascular procedures were not reported separately. PLR was analysed according to subgroups of quartiles, with the authors reporting a non-significant trend towards increased 30-day mortality in the quartiles 1 and 4 vs. quartiles 2 and 3 (7.1 % and 8.9 % vs. 0.0 % and 3.6 %, $p > 0.05$).

3.4. Outcomes relating to PLR in patients undergoing EVAR

2 studies reported outcomes in patients undergoing EVAR in relation to PLR, of which one study (Lareyre et al. 2019, described in the previous section) [29] reported on a combined OSR and EVAR cohort. 1 study observed increased mortality associated with elevated PLR, and 1 study did not observe a significant association.

The methodology used by Lecumberri et al. (2021) [27] is described in a previous section in relation to NLR. The same analysis was performed using PLR as the variable of interest. PLR had significant univariate predictive value on 2- and 5-year survival (HR 1.002 and 1.002 respectively, $p < 0.05$). However, when added to the predictive model PLR did not significantly improve model fit.

3.5. Outcomes relating to SII

Lecumberri et al. (2021, methodology described in a previous section) [27] repeated their analyses in patients undergoing EVAR for uAAA using SII as the variable of interest. Whilst they report that SII was significantly associated with 2- and 5-year survival, they report HR of 1.000 and 1.000 respectively and p values of 0.066 and 0.043 respectively. The addition of SII to their predictive model did not improve model fit.

3.6. Outcomes relating to SIG

Bradley et al. (2023, the authors of the present review) report the association between SIG and overall survival in a cohort of patients undergoing elective EVAR or F/B-EVAR, recruited retrospectively from 3 centres [33]. With a median follow-up of 68 months, increasing SIG (range 0–4) was associated with increased hazard of mortality; HR 1.20, 95 % CI 1.02–1.40, $p < 0.05$).

3.7. Methods used to subgroup patients

Subgrouping of patients is summarised in Table 3.

NLR was subgrouped by tertiles in 1 study (Ko et al. 2021 [25]), by ROC analysis in 4 studies(Lecumberri et al., 2021 [27], King et al. 2020 [28], Bath et al. 2019 [30], Kordzadeh et al. 2015 [31]), by absolute values based on previous literature [34] in 1 study (Appleton et al. 2014 [32]), and by the maximally selected log rank statistic technique in 1 study (Octeau et al. 2021 [26]).

PLR was subgrouped by quartiles in 1 study (Lareyre et al. 2019 [29]), and analysed as a continuous variable in 2 studies (Ko et al. 2021 [25], Lecumberri et al. 2021 [27]). SII was analysed as a continuous variable by Lecumberri et al. [27].

Table 3
Methods to subgroup patients in studies investigating the effect of the SIR on mortality following OSR/EVAR for AAA.

Authors	Subgrouping of NLR	Subgrouping of PLR	Subgrouping of SII
Bradley et al. (2023) [33]	–	–	–
Ko et al. (2021) [25]	Tertiles (T1 ≤ 2.41, 2.41 ≤ T2 ≤ 6.07, T3 > 6.07) & Continuous	Continuous	–
Octeau et al. (2021) [26]	NLR ≥3.6 (Maximally selected log rank statistic)	–	–
Lecumberri et al. (2021) [27]	NLR ≥3.0 (ROC curve)	Continuous	Continuous
King et al. (2020) [28]	NLR ≥4.0 (ROC curve)	–	–
Bath et al. (2019) [30]	Post-operative NLR ≥4.0 (ROC curve)	–	–
Lareyre et al. (2019) [29]	–	Quartiles (Q1 <91.5, 91.5 < Q2 < 120.8, 120.8 < Q3 < 163.3, Q4 > 163.3)	–
Kordzadeh et al. (2015) [31]	NLR ≥5.0 (ROC curve)	–	–
Appleton et al. (2014) [32]	NLR ≥5.0 (Previous literature [34])	–	–

3.8. Risk of bias assessment

The risk of bias assessment using the QUIPS tool is shown in supplemental appendix 1, with a summary of the assessment outcomes in the included studies in Table 4. High risk of bias was judged in 5 of 54 (9 %) domains, moderate risk in 32 of 54 (60 %) domains, and low risk in 17 of 54 (31 %) domains.

4. Discussion

The present review summarises the evidence base describing the prognostic value of NLR, PLR, SII, and SIG in patients undergoing intervention for AAA. The majority of studies investigating NLR described an association between elevated NLR and increased mortality, at a range of follow-up points, in patients undergoing both OSR and EVAR. This is in keeping with observations from other authors in non-cancer populations. Regarding PLR, the association with outcomes is less well defined, with fewer studies reporting a prognostic role. SII did not appear to offer prognostic value in this patient group, though there is a relative lack of evidence. SIG was associated with inferior prognosis, and is attractive as a measure due to it encompassing 2 different mechanistic pathways.

The mechanism by which activation of the SIR produces inferior survival in patients with AAA is not well defined, however is likely reflective of increased risk of cardiovascular event in a patient group already prone to cardiovascular morbidity [9]. Whilst the association between inflammation and atherosclerosis to date has largely been in the research setting, an association between the clinically measurable NLR and both generalised atherosclerosis and impaired outcome in cerebrovascular and coronary artery disease is described [35]. Endothelial microinjury triggers a localised inflammatory response, and subsequent lipid deposition accelerates the progression to atherosclerotic plaque. Moreover, the formation of a necrotic plaque core is itself an inflammatory event, which allows micro- and macro-calcification of plaque to occur.

In an attempt to improve cardiovascular morbidity and mortality, modulation of the SIR in patients with cardiovascular disease is beginning to emerge as a promising strategy, though one which is currently in its infancy. The CANTOS trial showed a benefit to IL-1β blockade in patients with ischaemic heart disease both in a reduction in cardiovascular events [36] and reduced rate of incident lung cancer [37]. However, this immunomodulation resulted in an increased rate of infection in the treatment group. Eagerly awaited follow-up studies targeting alternative cytokines may pave the way to clinical implementation of immunomodulation in this setting. Translating this strategy to other "high risk" patient groups, for example those with other manifestations of arterial disease, is of particular interest. In patients with AAA, perioperative methylprednisolone has been investigated with results suggesting mitigation of the post-operative inflammatory response and improved recovery [38,39], though the effects on long-term outcomes are unreported.

In patients undergoing EVAR, early activation of the SIR may manifest clinically as the post-implantation syndrome (PIS), which appears to confer inferior mid-term outcomes [40]. PIS is influenced by a variety of factors, including inflammatory response to graft material, mechanical disruption of thrombus, and endothelial disruption. Whilst the precise mechanism of PIS is incompletely understood, there appears to

Table 4
Risk of bias summary judgements (from QUIPS tool) for the studies included in the final review.

Study	Study Participation	Study Attrition	Prognostic Factor Measurement	Outcome Measurement	Study Confounding	Statistical Analysis and Reporting
Bradley et al (2023)[33]						
Ko et al (2021)[25]						
Octeau et al (2021)[26]						
Lecumberri et al (2021)[27]						
King et al (2020)[28]						
Bath et al (2019)[30]						
Lareyre et al (2019)[29]						
Kordzadeh et al (2015)[31]						
Appleton et al (2014)[32]						

Green – low risk of bias. Amber – moderate risk of bias. Red – high risk of bias

be an IL-6 dependent inflammatory response which may be due to thrombus disruption either due to stent-graft deployment or wire trauma. Both aneurysm sac thrombus and vascular endothelium are known to be rich in IL-6, and elevated serum IL-6 has been observed in patients with PIS. In patients undergoing OSR, the massive inflammatory response provoked by extensive dissection makes the subtleties of the inflammatory environment more challenging to characterise. The effect of PIS on systemic inflammation-based scoring systems is not described, however may confound outcomes and is an area for future research.

The majority of the studies included in the present review reported outcomes on patients undergoing intervention for infrarenal AAA; patients undergoing intervention for juxta- or para-renal AAA are underrepresented. Both open and endovascular repairs of these aneurysms are more complex procedures than for infrarenal AAA, carrying a different risk profile. Open repair of complex aneurysms is typically a longer operation with a greater degree of dissection, and may produce a greater peak in the well-described post-operative inflammatory cytokine response [41]. F/B-EVAR are typically longer procedures than EVAR, with increased contrast and radiation doses. Contrast is known to induce an inflammatory response [42], and a cytokine response following high doses of radiation is described [43]. The acute inflammatory insult following these procedures may be potentiated by underlying chronic activation of the SIR, and this relationship warrants further investigation.

There is no validated cutoff of NLR, PLR, or SII to indicate pathological state. Regarding NLR, typical cutoff values are 3.0 and 5.0, which have been extensively studied in patients with cancer [6]. Only 2 of the studies included in this review used 5.0 as a cutoff based on previous results, although 2 studies used 3.0 and 5.0 respectively based on ROC analysis. A potential benefit to SIG is that it provides a categorical method of subgrouping patients therefore can be readily compared in clinical and research settings. Determining optimal values is a key component to allow the translation of these scoring systems from the research sector to clinically useful parameters.

5. Limitations

There were 3 studies [44–46] which the authors were unable to obtain in full in the English language, which introduces evidence selection bias into the findings of this review. 2 studies had relevant patient populations however included only pooled outcomes on patients with AAA and non-AAA pathologies, and so were discounted. The studies included in the review are subject to significant bias due to the inherent limitations in their study design (supplemental appendix 1). Inter-study heterogeneity precluded meaningful quantitative analysis. Data on the association between inflammatory parameters and baseline clinicopathological, such as age, sex, and potentially confounding medications (e.g. statins, anti-platelet agents, anticoagulants) were not widely available, and this is a potential source of bias. The present review is limited by the inter-study heterogeneity in the included studies. The patients encompass a heterogenous cohort, with both emergency and elective cases, pre- and post-operative blood sampling, and different treatment modalities. Each of these factors may confound the measurement of the systemic inflammatory response, and is an important limitation which may be addressed in further prospective studies.

6. Conclusions

NLR provides prognostic value in patients undergoing intervention for AAA. PLR and SII currently have insufficient evidence to support their role. mGPS is unreported and is a potentially valuable tool in prognostication. Further prospective investigation of inflammation-based prognostic scoring systems, in particular considering potentially confounding factors and clinically meaningful outcomes, in patients with AAA and other cardiovascular disease is required. These studies should aim to build on the foundation describing these prognostic factors in patients with cancer.”.

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Declaration of competing interest

Nicholas A Bradley, Campbell S D Roxburgh, Donald C McMillan, and Graeme J K Guthrie declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.surge.2024.08.014.

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