The Relationship Between Peri-Operative Systemic Inflammation and Survival in Patients With Abdominal Aortic Aneurysm

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Background: An association between preoperative markers of systemic inflammation and inferior mortality following abdominal aortic aneurysm (AAA) repair has been observed. The prognostic value of the postoperative inflammatory response remains unreported in patients with AAA. This study aimed to describe the association between the perioperative inflammatory response and mortality in patients undergoing endovascular aneurysm repair and open surgical repair (OSR) for infrarenal AAA.

Methods: Consecutive patients undergoing either emergency (endovascular aneurysm repair or OSR) or elective (OSR) intervention for infrarenal AAA were retrospectively recruited from 3 centers. Preoperative systemic inflammation was assessed using the modified Glasgow Prognostic Score. Day 3 postoperative C-reactive protein (CRP) ($\leq$300 mg/L, $>$300 mg/L) was chosen as the covariate of interest. The primary outcome was 30-day mortality in the emergency cohort and 12-month mortality in the elective cohort.

Results: There were 167 emergency cases (120 (72%) OSR) and 207 elective (207 (100%) OSR) cases, with a median (interquartile range) follow-up of 85 (52) months in the emergency cohort and 63 (57) months in the elective cohort. There were 56% versus 44% of patients in the emergency cohort day 3 CRP $\leq$300 mg/l versus $>$300 mg/L compared with 82% versus 18% of patients in the elective cohort ($P < 0.001$). On univariate binary logistic regression analyses in the emergency cohort, open repair ($P < 0.05$), preoperative modified Glasgow Prognostic Score 2 ($P < 0.05$), postoperative mesenteric ischemia ($P < 0.01$), and day 3 postoperative CRP $>$300 mg/L ($P < 0.05$) were associated with increased odds of 30-day mortality. On multivariate binary logistic regression analyses, only preoperative modified Glasgow Prognostic Score 2 (odds ratio [OR]: 2.11, 95% confidence interval [CI]: 1.12–3.98, $P < 0.05$) retained independent association with 30-day mortality. In the elective cohort, mean (95% CI) survival in the day 3 CRP $\leq$300 mg/l versus $>$300 mg/L was 112.0 (101.8–122.2) months versus 67.2 (54.1–80.2) months ($P < 0.001$). On univariate binary logistic regression analyses in the elective cohort, age $\geq$75 ($P < 0.05$), ischemic heart disease ($P < 0.05$), and day 3 postoperative CRP $>$300 mg/L ($P < 0.001$) were associated with increased odds of 12-month mortality. On multivariate binary logistic regression analyses, both age $\geq$75 (OR: 5.15, 95% CI: 1.25–21.30, $P < 0.05$) and day 3 postoperative CRP $>$300 mg/L (OR: 15.68, 95% CI: 3.61–68.15, $P < 0.001$) retained independent association with 12-month mortality.

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Conclusions: Preoperative and postoperative markers of systemic inflammation were independently associated with inferior survival following emergency and elective repair of AAA, respectively. Further investigation of the perioperative systemic inflammatory response is warranted in this patient group, with a particular focus on identifying targets for intervention.

INTRODUCTION

Abdominal aortic aneurysm (AAA) remains an important health condition; the estimated UK prevalence is 1.5%, rising to approximately 4% in males aged over 65.[1] Intervention for AAA generally consists of either open surgical repair (OSR) or endovascular aneurysm repair (EVAR). In the elective setting, repair is a prophylactic measure to remove the potential of aneurysm rupture, which itself carries high morbidity and mortality.

Activation of the systemic inflammatory response (SIR) has emerged as a key etiological and prognostic factor in a range of illnesses, including cardiovascular disease.[2] Elevated magnitude of the SIR, measured preoperatively, appears to be associated with inferior prognosis in patients with vascular disease.[3,4] Regarding AAA, the majority of literature report outcomes in patients undergoing elective intervention, due to the potentially confounding effect of aneurysm rupture on the SIR. Regardless, a range of preoperative measures of the SIR appear to be associated with prognosis following the intervention for AAA.[3] These findings are consistent with those observed in patients undergoing intervention for cancer.[5,6]

The prognostic value of the postoperative SIR is generally less well reported in all conditions as compared with the preoperative SIR, likely due to the confounding effect that a surgical insult has on systemic inflammation. The postoperative Glasgow Prognostic Score (poGPS) describes the acute phase response following major surgical intervention.[7] There appears to be an association between poGPS and survival (both short-term and long-term) in patients undergoing resection for colorectal cancer, as well as in nonsurgical conditions.[7,8] Watt et al. described a prognostic role for poGPS measured on the third postoperative day, corresponding to a typically expected peak in postoperative C-reactive protein (CRP).[7] Additionally, they reported the predictors of an elevated poGPS, which include preoperative systemic inflammation, and tumor site.[9] Furthermore, maximal CRP appears to confer inferior survival in an unselected cohort of elderly patients presenting to acute medical services.[10] It appears that the magnitude of the SIR following aortic surgery is much greater than following colorectal cancer surgery; therefore, the use of poGPS in an AAA cohort may be limited.[11] Low skeletal muscle mass and function (sarcopenia), as assessed by computed tomography (CT)-derived body composition (CT-BC), have been widely reported to be associated with inferior prognosis in both cardiovascular and noncardiovascular diseases.[12,13] Inflammation is an etiological component of sarcopenia, and routinely available measures of the preoperative SIR appear to be associated with CT-BC parameters in patients with AAA.[14,15] The relationship between sarcopenia and magnitude of the postoperative SIR is poorly reported across all disease states. The prognostic role of the postoperative SIR remains unreported in patients with AAA.

This study, therefore, aimed to describe the prognostic role of the perioperative SIR in patients undergoing both emergency and elective intervention for AAA, to evaluate potential factors associated with elevated magnitude of the postoperative SIR, and to evaluate the association between the perioperative SIR and preoperative CT-BC muscle parameters.

MATERIALS AND METHODS

Patient Eligibility and Data Collection

Patients were retrospectively identified from existing theater records at 3 large tertiary referral centers in Scotland, UK, representing cases drawn from 3 health boards (NHS Grampian, NHS Lanarkshire, and NHS Tayside). Specific procedural techniques were at the discretion of each institution, though practice was broadly similar between sites throughout the study period. Clinical, demographic, and comorbidity data were recorded from electronic case records and patients' community health records. Age ($<$75 years, $\geq$75 years), body mass index (BMI) ($<$25 kg/m^2, $\geq$25 kg/m^2), and hemoglobin ($<$135 g/L, $\geq$135 g/L in males, $<$120 g/L, $\geq$120 g/L in females) were considered as categorical variables. BMI was not available for emergency cases. Mesenteric ischemia was defined as compromised viability at any level of the gastrointestinal tract necessitating resection, thought to be secondary to ischemia, and diagnosed clinically by both a consultant vascular surgeon and consultant general surgeon. Patients with active malignancy, active infection, juxta- or para-renal aneurysms, isolated iliac aneurysms, or

those prescribed immunomodulatory medications, were excluded due to the potential confounding. Additionally, patients with missing postoperative inflammatory parameters of interest were excluded. West of Scotland Research Ethics Committee approval was obtained for this study (reference 21/WS/0146; approval granted on November 23, 2021).

Emergency Cohort

Consecutive cases undergoing EVAR or OSR to treat infrarenal ruptured AAA (rAAA) between January 1, 2011, and December 31, 2023, were screened for inclusion. rAAA was defined as CT-proven aneurysm rupture, confirmed by consultant radiologist; patients with ''impending rupture'' or symptomatic AAA were not eligible for inclusion. In addition, patients on whom repair was attempted but abandoned intraoperatively were excluded. All patients in the emergency cohort achieved a minimum follow-up of 30 days from the date of surgery.

Elective Cohort

Due to likely discharge prior to blood sampling on postoperative day 3, patients undergoing elective endovascular intervention were excluded. Therefore, consecutive cases undergoing elective OSR to treat infrarenal AAA between January 1, 2015, and December 31, 2022, were screened for inclusion. Patients with ''impending rupture'' of AAA on CT, symptomatic AAA, or clinical suspicion of inflammatory/mycotic AAA were excluded. All patients in the elective cohort achieved a minimum follow-up of 12 months from the date of surgery.

Outcomes of Interest

The primary outcome in the emergency cohort was 30-day mortality, and the primary outcome in the elective cohort was 12-month mortality. Both of these outcomes were chosen as they were felt to represent a clinically relevant timepoint in each cohort, and all patients achieved the required minimum follow-up. Outcome data were obtained from the Community Health Index registry, a routinely available registry maintained at a national health board level and populated from both primary and secondary care data. Specific cause of death was not available from this registry.

Inflammatory Profiling

The authors originally intended to examine the day 3 poGPS as the covariate of interest, however, on preliminary analyses it became apparent that in excess of 95% of patients in both cohorts had a day 3 poGPS = 2, precluding any meaningful analyses. Therefore, day 3 CRP was chosen as the covariate of interest, and patients were subgrouped for analysis ($\leq$300 mg/L, >300 mg/L). These thresholds were chosen based on close relation to the median value in each cohort (Table I). The third postoperative day was chosen due to this being the typical peak value for CRP following major surgery.[16,17] Day 3 albumin was also examined, with thresholds of $\leq$25 g/L, >25 g/L chosen based on median values. Preoperative activation of the SIR was assessed using the modified Glasgow Prognostic Score (mGPS; 0, 1, 2), calculated from admission blood results as described previously (Supplemental Table 1).[5] All blood tests were performed every day routinely as part of existing patient care. Patients with missing day 3 CRP were excluded.

CT-BC Analysis

CT-BC analysis was performed on preoperative planning CTs at the L3 vertebral level using the manual segmentation method in ImageJ, v1.53, as described previously.[13] Skeletal muscle mass was assessed using the skeletal muscle index (SMI), and skeletal muscle function was assessed using the skeletal muscle density (SMD). Thresholds previously reported (Martin et al.[18]) were applied to these continuous CT-BC parameters to enable subgrouping of patients for analysis. Due to the extent of retroperitoneal hematoma in rAAA limiting the measurement of skeletal muscle in >90% of cases, CT-BC analyses were only performed on the elective cohort.

Statistical Analyses

Other than initial comparisons, separate analyses were performed on the emergency and elective cohorts. Differences between categorical variables were compared using the linear-by-linear chi-squared test. Covariates of interest were examined using binary logistic regression, where covariates with univariate $P < 0.05$ were included in a multivariate model. In the multivariate models, the risk of multicollinearity was assessed using the variance inflation factor, with variance inflation factor < 5 considered acceptable in keeping with typical practice.[19] Time-to-event analyses were calculated using the Kaplan–Meier method, with differences between subgroups assessed using the log-rank test. Where time to event survival data did not reach a median survival, the mean (95% confidence interval [CI]) values are reported. Data are presented as median (interquartile range, IQR) unless otherwise

Table I. The association between clinicopathological factors and survival in patients undergoing emergency or elective open surgical repair of infrarenal AAA

Covariate	Emergency repair ($n = 167$)	Elective open surgical repair ($n = 207$)	P	Emergency repair ($n = 167$) Day 3 CRP ≤300 mg/L ($n = 94$, 56%)	Emergency repair ($n = 167$) Day 3 CRP >300 mg/L ($n = 73$, 44%)	P	Elective open surgical repair ($n = 207$) Day 3 CRP ≤300 mg/L ($n = 170$, 82%)	Elective open surgical repair ($n = 207$) Day 3 CRP >300 mg/L ($n = 37$, 18%)	P
Age ≥ 75	91 (55%)	61 (30%)	**<0.001**	53 (56%)	38 (52%)	0.58	51 (30%)	10 (27%)	0.72
Female sex	26 (16%)	16 (8%)	**<0.05**	15 (16%)	11 (15%)	0.91	15 (9%)	1 (3%)	0.21
Ischemic heart disease	35 (22%)	48 (23%)	0.80	19 (21%)	16 (23%)	0.78	31 (18%)	17 (46%)	**<0.001**
Diabetes mellitus	13 (8%)	36 (18%)	**<0.05**	8 (9%)	5 (7%)	0.71	30 (18%)	6 (16%)	0.82
Cigarette smoker	39 (25%)	71 (35%)	**<0.05**	18 (21%)	21 (30%)	0.15	56 (33%)	15 (41%)	0.39
Statin use	88 (56%)	154 (75%)	**<0.001**	47 (54%)	41 (59%)	0.50	124 (74%)	30 (81%)	0.36
Open surgical repair	120 (72%)	-	-	51 (54%)	69 (95%)	**<0.001**	-	-	-
BMI ≥25 kg/m^2	-	146 (71%)	-	-	-	-	116 (69%)	30 (81%)	0.13
Low SMI[a]	-	102 (50%)	-	-	-	-	81 (48%)	21 (58%)	0.27
Low SMD[a]	-	46 (23%)	-	-	-	-	39 (23%)	7 (19%)	0.62
Low preop Hb	107 (65%)	38 (19%)	**<0.001**	66 (70%)	41 (57%)	0.08	33 (20%)	5 (14%)	0.38
Preop mGPS			**<0.001**			0.74			0.66
0	50 (41%)	152 (89%)		31 (44%)	19 (37%)		128 (89%)	24 (86%)	
1	43 (35%)	18 (10%)		22 (31%)	21 (40%)		14 (10%)	4 (14%)	
2	30 (24%)	1 (1%)		18 (25%)	12 (23%)		1 (1%)	0 (0%)	
Postop mesenteric ischemia	9 (5%)	0 (0%)	**<0.001**	3 (3%)	6 (8%)	0.15	-	-	-
Median (IQR) day 3 albumin (g/L)	24 (6)	25 (4)	**<0.001**	25 (7)	22 (6)	**<0.01**	26 (4)	25 (4)	0.21
Median (IQR) day 3 CRP (mg/L)	292 (131)	250 (89)	**<0.001**	-	-	-	-	-	-
Thirty-day mortality	35 (21%)	3 (1%)	**<0.001**	13 (14%)	22 (30%)	**<0.05**	1 (1%)	2 (5%)	**<0.05**
Twelve-month mortality[b]	-	10 (5%)	-	-	-	-	3 (2%)	7 (19%)	**<0.001**

Data are presented as n (%) unless specified. P values for categorical covariates were generated through linear-by-linear chi-squared analyses comparing absolute proportions of covariates within each subgroup based on presentation type or day 3 CRP, and for continuous covariates using independent samples Mann–Whitney U test. Missing data selectively excluded from relevant analyses; % calculated based on included cases not total cases.

Bold text refers to statistically significant results.

[a]SMI and SMD not reported in emergency cases due to retroperitoneal hematoma precluding effective measurement.

[b]Twelve-month mortality not reported in emergency patients as not all patients achieved the necessary minimum follow-up.

stated. Missing data were selectively excluded from relevant analyses on a case-by-case basis. Analyses were performed using IBM SPSS (version 28.0, IBM, NY). *P* values < 0.05 were considered statistically significant.

RESULTS

There were 511 (222 emergency, 289 elective) procedures screened for inclusion during the study period. Following exclusions, the final study cohort consisted of 167 emergency cases and 207 elective cases. Median (IQR) follow-up was 85 (52) months in the emergency cohort and 63 (57) months in the elective cohort. During the follow-up period, there were 92 deaths in emergency patients and 57 deaths in elective patients. The distribution of patients in day 3 CRP subgroups between emergency and elective cases is shown in Figure 1; the proportion of patients with day 3 CRP ≤300 mg/L vs. >300 mg/L was 56% vs. 44% of patients in the emergency cohort compared with 82% vs. 18% of patients in the elective cohort ($P < 0.001$).

Table I shows the clinical and pathological covariates subgrouped by procedure priority and postoperative CRP. Compared with the elective cohort, the emergency cohort were typically older ($P < 0.001$), with a higher proportion of females ($P < 0.05$), a lower rate of diabetes mellitus ($P < 0.05$), cigarette smoking ($P < 0.05$), and statin use ($P < 0.001$) and had a greater rate of low preoperative hemoglobin ($P < 0.001$), postoperative mesenteric ischemia ($P < 0.001$), and 30-day mortality ($P < 0.001$). Median (IQR) day 3 CRP was 292 (131) mg/L in emergency cases compared with 250 (89) mg/L in elective cases ($P < 0.001$), and median (IQR) day 3 albumin was 24 (6) g/L in emergency cases compared with 25 (4) g/L in elective cases ($P < 0.001$). In emergency cases, day 3 CRP >300 mg/L was associated with an increased rate of OSR ($P < 0.001$) and with 30-day mortality ($P < 0.05$). In elective cases, day 3 CRP >300 mg/L was associated with an increased rate of ischemic heart disease ($P < 0.010$) and with an increased 30-day ($P < 0.05$) and 12-month ($P < 0.001$) mortality.

Kaplan–Meier survival plots are shown in Figures 2 and 3, and Supplemental Figure 1. In the combined emergency and elective cohorts, mean (95% CI) survival in the day 3 CRP ≤300 mg/l versus >300 mg/L was 97.6 (89.4–105.8) months versus 67.9 (56.9–78.8) months ($P < 0.001$, Fig. 2). In the elective cohort, mean (95% CI) survival in the day 3 CRP ≤300 mg/L versus >300 mg/L was 112.0 (101.8–122.2) months versus 67.2 (54.1–80.2) months ($P < 0.001$, Fig. 3). In the subgroup of patients in the elective cohort with low SMI, mean (95% CI) survival in the day 3 CRP ≤300 mg/l versus >300 mg/L was 112.1 (97.9–126.4) months versus 65.4 (47.3–83.4) months ($P < 0.01$, Supplemental Fig. 1). Table II displays the associations between clinicopathological factors and 30-day mortality in the emergency cohort. In patients who suffered 30-day mortality, there was an increased prevalence of open repair (86% vs. 68%, $P < 0.05$), preoperative mGPS 2 (46% vs. 20%, $P < 0.05$), and postoperative mesenteric ischemia (15% vs. 3%, $P < 0.01$). Sixty-three percent of patients who suffered 30-day mortality had day 3 CRP >300 mg/L, compared with 39% of 30-day survivors ($P < 0.05$). On univariate binary logistic regression analyses, open repair ($P < 0.05$), preoperative mGPS 2 ($P < 0.05$), postoperative mesenteric ischemia ($P < 0.01$), and day 3 postoperative CRP > 300 mg/L ($P < 0.05$) were associated with increased odds of 30-day mortality. On multivariate binary logistic regression analyses, only preoperative mGPS 2 (odds ratio [OR]: 2.11, 95% CI: 1.12–3.98, $P < 0.05$) retained independent association with 30-day mortality.

Table III displays the associations between clinicopathological factors and 12-month mortality in the elective cohort. Patients who suffered 12-month mortality were typically older (age ≥75; 60% vs. 28%, $P < 0.05$), had a greater prevalence of comorbid ischemic heart disease (50% vs. 22%, $P < 0.05$), and had a greater prevalence of low SMI (80% vs. 49%, $P < 0.05$). Seventy percent of patients who suffered 12-month mortality had day

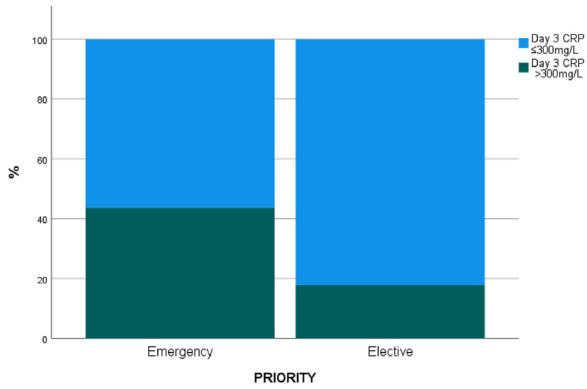
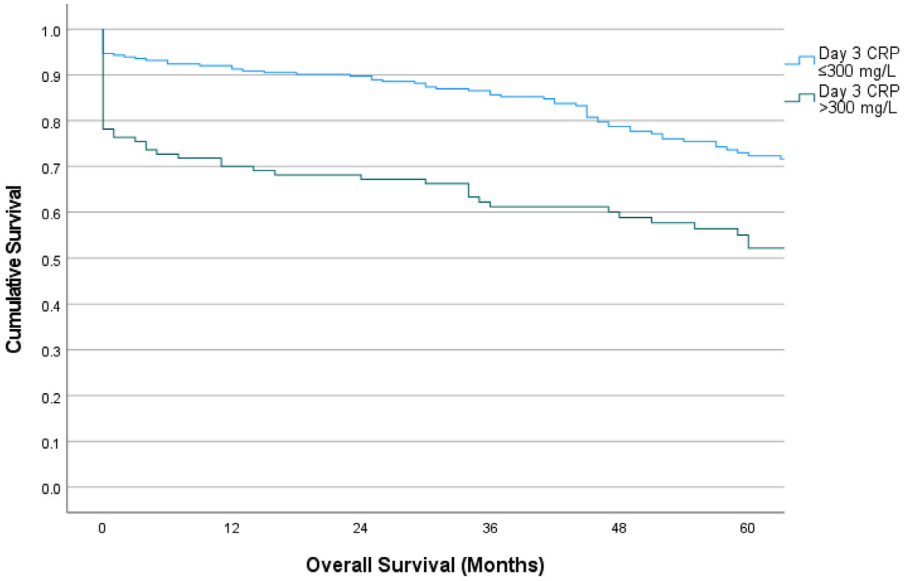


Fig. 1. A comparison of postoperative day 3 CRP in patients undergoing emergency ($n = 167$) and elective open surgical ($n = 207$) repair of infrarenal AAA. $P < 0.001$. *P* value was generated through linear-by-linear chi-squared analyses comparing absolute proportions within each subgroup based on day 3 CRP.



	Number at Risk					
Months	**0**	**12**	**24**	**36**	**48**	**60**
Day 3 CRP ≤300mg/L	264	241	233	194	154	112
Day 3 CRP >300mg/L	110	77	73	59	53	39

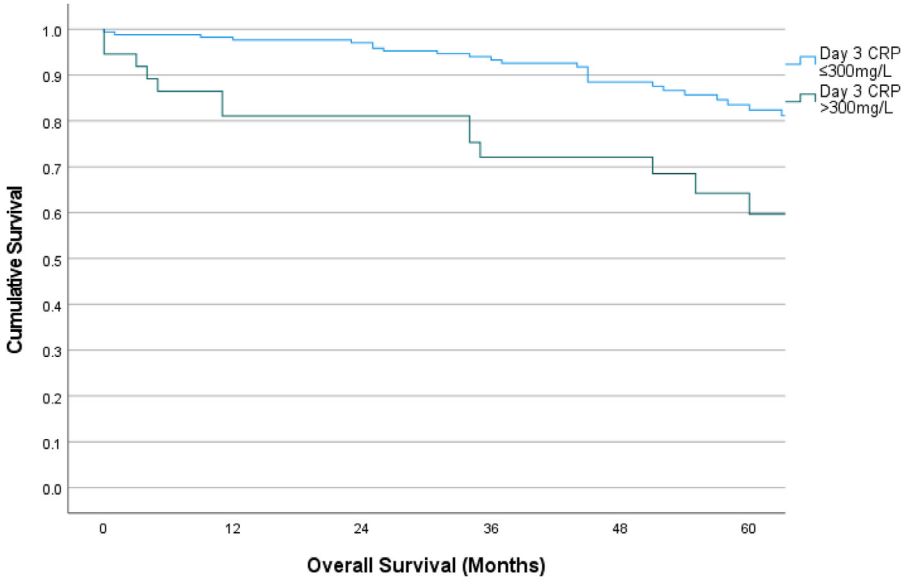
Fig. 2. Kaplan–Meier survival plots and life table of day 3 CRP subgroups in patients undergoing emergency and elective open surgical repair of infrarenal AAA ($n = 374$). $P < 0.001$ (log-rank method).

3 CRP > 300 mg/L, compared with 15% of 12-month survivors ($P < 0.01$). On univariate binary logistic regression analyses, age ≥ 75 ($P < 0.05$), ischemic heart disease ($P < 0.05$), and day 3 postoperative CRP > 300 mg/L ($P < 0.001$) were associated with increased odds of 12-month mortality. On multivariate binary logistic regression analyses, both age ≥ 75 (OR: 5.15, 95% CI: 1.25–21.30, $P < 0.05$) and day 3 postoperative CRP > 300 mg/L (OR: 15.68, 95% CI: 3.61–68.15, $P < 0.001$) retained independent association with 12-month mortality.

DISCUSSION

The results of this study describe the novel association between perioperative markers of the SIR and inferior mortality outcomes following intervention for AAA. In the emergency setting, preoperative mGPS was independently associated with early mortality and in the elective open setting an elevated postoperative CRP was independently associated with late mortality. Therefore, both preoperative and postoperative monitoring of the SIR may be warranted in patients undergoing surgery for AAA.

In this study, 24% of patients with an emergency presentation had mGPS 2 on admission, despite the likely relatively short time period between the onset of symptoms and blood sampling. This highlights the marked inflammatory response produced by aneurysm rupture itself, even when the effect of surgical repair is not taken into consideration. Furthermore, 18% of patients with an elective presentation had an elevated day 3 CRP (>300 mg/L) and was independently associated with a poorer 12-month survival. In this setting, the magnitude of inflammatory response was likely caused by the surgical insult is analogous to the acute severe illness in other cohorts. Indeed, an association between the magnitude of systemic inflammation and short-term outcomes in cancer and critical illness has been described previously; Lobo and colleagues reported inferior survival and increased risk of organ failure associated with elevated CRP in an unselected cohort of patients admitted to intensive care.[20] Similarly, Ho and colleagues reported increased risk of in-hospital death associated with high CRP in an unselected cohort of patients



	Number at Risk					
Months	**0**	**12**	**24**	**36**	**48**	**60**
Day 3 CRP ≤300mg/L	170	167	165	132	105	73
Day 3 CRP >300mg/L	37	30	30	22	21	14

Fig. 3. Kaplan–Meier survival plots and life table of day 3 CRP subgroups in patients undergoing elective open surgical repair of infrarenal AAA ($n = 207$). $P < 0.001$ (log-rank method).

admitted to intensive care.[21] Furthermore, CRP appears to predict disease severity and outcomes in infective illnesses,[22–24] and maximal CRP appears to influence prognosis in patients with pneumonia.[25] Lastly, the development of an acute severe illness necessitating critical care stay is known to influence long-term survival outcomes.[26–28] Therefore, the magnitude of preoperative and postoperative SIRs are likely to be important factors in determining clinical outcome.

In this study, the magnitude of the postoperative SIR in both emergency (44%) and elective (18%) cases was greater than previous reports of peak CRP following open aortic surgery.[11] However, the evidence base reviewed by Watt et al. was limited by small numbers (234 patients in 9 studies) and heterogenous postoperative sampling times. Irrespectively, it appears that the CRP response following open aortic surgery exceeds that of the majority of abdominal surgery and is comparable to major upper gastrointestinal resection and cardiac surgery.[11] The extent of dissection, operative time, and requirement for a period of infrarenal ischemia associated with OSR of AAA are all likely to contribute to the significant inflammatory response to surgery. Therefore, alternative thresholds of day 3 CRP were used in this study. The complexities of this acute phase protein response in different surgical settings highlight the importance of developing additional operation-specific inflammation-based prognostic scoring systems and monitoring this response, which may ultimately provide a measure by which innovations in treatment can be tested.

The mechanism by which activation of the SIR results in an inferior prognosis is poorly understood. The association between risk of cardiovascular event and inflammation is well described[29]; however, this is typically described in patients with chronic low-grade inflammation which results in increased burden of systemic atherosclerosis. Whether a single major inflammatory insult, such as aneurysm repair or rupture, predisposes patients to increased risk of cardiovascular event is unknown. Similarly, the development of sustained low-grade inflammation following the initial insult is another potential mechanistic pathway.

The determinants of the postoperative SIR are poorly understood but provide a legitimate

Table II. The association between clinicopathological factors, day 3 postoperative CRP, and 30-day mortality in patients undergoing emergency repair of ruptured infrarenal AAA ($n = 167$)

				Univariate[b]			Multivariate[b]			
Covariate	Thirty-day survivor ($n = 132$)	Thirty-day mortality ($n = 35$)	P[a]	OR	95% CI	P	OR	95% CI	P	Variance inflation factor
Age $\geq$ 75	71 (54%)	20 (57%)	0.72	1.15	0.54–2.43	0.72	-	-	-	-
Female sex	22 (17%)	4 (12%)	0.48	0.67	0.21–2.08	0.48	-	-	-	-
Ischemic heart disease	27 (21%)	8 (28%)	0.44	1.45	0.58–3.61	0.44	-	-	-	-
Diabetes mellitus	8 (6%)	5 (17%)	0.06	3.03	0.91–10.02	0.07	-	-	-	-
Cigarette smoker	33 (26%)	6 (21%)	0.57	0.75	0.28–2.01	0.57	-	-	-	-
Statin use	71 (56%)	17 (61%)	0.61	1.24	0.54–2.86	0.61	-	-	-	-
Open surgical repair	90 (68%)	30 (86%)	**< 0.05**	2.80	1.02–7.23	**< 0.05**	1.51	0.43–5.34	0.53	1.279
Low preop Hb	84 (64%)	23 (68%)	0.66	1.20	0.54–2.66	0.66	-	-	-	-
Preop mGPS			**< 0.05**	1.92[c]	1.08–3.43	**< 0.05**	2.11[c]	1.12–3.98	**< 0.05**	1.054
0	43 (43%	7 (29%)								
1	37 (37%)	6 (25%)								
2	19 (20%)	11 (46%)								
Postop mesenteric ischemia	4 (3%)	5 (15%)	**< 0.01**	5.52	1.40–21.83	**< 0.01**	1.91	0.37–10.02	0.44	1.060
Day 3 albumin			0.18	0.57	0.25–1.30	0.18	-	-	-	-
$\leq$25 g/L	73 (58%)	24 (71%)								
>25 g/L	53 (42%)	10 (29%)								
Day 3 CRP			**< 0.05**	2.69[c]	1.25–5.81	**< 0.05**	2.14[c]	0.72–6.37	0.17	1.279
$\leq$300 mg/L	81 (61%)	13 (37%)								
>300 mg/L	51 (39%)	22 (63%)								

Bold text refers to statistically significant results.

VIF, variance inflation factor.

[a]Data presented as absolute value (% of total). P values were generated through linear-by-linear chi-squared analyses comparing proportions between subgroups based on 30-day mortality.

[b]Data presented are odds of suffering 30-day mortality; odds ratio (OR), 95% CI, P value generated through binary logistic regression, with the risk of multicollinearity assessed using the VIF.

[c]OR and 95% CI pertain to preop mGPS 2 and day 3 CRP >300 mg/L compared with the other categories as reference categories.

Table III. The association between clinicopathological factors, day 3 postoperative CRP, and 12-month mortality in patients undergoing elective open surgical repair of infrarenal AAA ($n = 207$)

				Univariate[b]			Multivariate[b]			
Covariate	Twelve-month survivor ($n = 197$)	Twelve-month mortality ($n = 10$)	P[a]	OR	95% CI	P	OR	95% CI	P	Variance inflation factor
Age $\geq$ 75	55 (28%)	6 (60%)	**<0.05**	3.87	1.05−14.25	**<0.05**	5.15	1.25−21.30	**<0.05**	1.001
Female sex	16 (8%)	0 (0%)	0.35	-	-	-	-	-	-	-
Ischemic heart disease	43 (22%)	5 (50%)	**<0.05**	3.56	1.00−12.86	0.05	-	-	-	-
Diabetes mellitus	35 (18%)	1 (10%)	0.52	0.51	0.06−4.17	0.53	-	-	-	-
Cigarette smoker	68 (35%)	3 (30%)	0.76	0.81	0.20−3.22	0.76	-	-	-	-
Statin use	146 (75%)	8 (80%)	0.72	1.34	0.28−6.54	0.72	-	-	-	-
BMI $\geq$ 25 kg/m^2	139 (71%)	7 (70%)	0.95	0.96	0.24−3.83	0.95	-	-	-	-
Low SMI	94 (49%)	8 (80%)	**<0.05**	4.26	0.88−20.56	0.07	-	-	-	-
Low SMD	43 (22%)	3 (30%)	0.56	1.51	0.37−6.07	0.57	-	-	-	-
Low pre-op Hb	36 (19%)	2 (20%)	0.91	1.10	0.22−5.39	0.91	-	-	-	-
Pre-op mGPS			0.18	-	-	-	-	-	-	-
0	143 (88%)	9 (100%)								
1	18 (11%)	0 (0%)								
2	1 (1%)	0 (0%)								
Day 3 albumin			0.09	0.28	0.06−1.38	0.12	-	-	-	-
$\leq$25 g/L	88 (49%)	7 (78%)								
>25 g/L	90 (51%)	2 (22%)								
Day 3 CRP			**<0.001**	12.99[c]	3.18−53.01	**<0.001**	15.68[c]	3.61−68.15	**<0.001**	1.001
$\leq$300 mg/L	167 (85%)	3 (30%)								
>300 mg/L	30 (15%)	7 (70%)								

Bold text refers to statistically significant results.

[a]Data presented as absolute value (% of total). P values generated through linear-by-linear chi-squared analyses comparing proportions between subgroups based on 12-month mortality.

[b]Data presented are odds of suffering 12-month mortality; odds ratio (OR), 95% CI, P value generated through binary logistic regression, with the risk of multicollinearity assessed using the VIF. Due to lack of any females or patients with pre-op mGPS >0 experiencing 12-month mortality, meaningful logistic regression could not be performed.

[c]OR and 95% CI pertain to CRP >300 mg/L compared with CRP $\leq$ 300 mg/L as a reference category.

therapeutic target. In particular, the association between skeletal muscle mass and quality as measured by CT-BC, and the development of increased magnitude of the SIR in the acute and chronic setting, is poorly described. This study did not demonstrate a relationship between the postoperative SIR and CT-BC parameters. Reisinger et al. reported on a cohort of patients undergoing elective resection colorectal cancer, where patients with low skeletal muscle mass developed a more marked postoperative inflammatory response as measured by calprotectin but not CRP or IL-6.[30] Calprotectin is not measured routinely in patients with AAA, however, this may form the basis of future studies.

To date, immunomodulation in cardiovascular disease has primarily taken place in the nonemergency setting,[31,32] with increased risk of infection as the major drawback. Identifying patients at risk of a greater postoperative SIR may allow for perioperative adjunctive therapy, such as steroid use, in an attempt to mitigate this response. Preoperative methylprednisolone appears to reduce the rate of postimplantation syndrome and improve recovery following elective EVAR; however, this has not yet translated to widespread clinical practice.[33] Data on perioperative steroid use in the present cohort were not available; this is a potential area for further investigation.

Limitations

The issue of reverse causality in measuring systemic inflammation is an important consideration and limitation of this study, in particular in the emergency cohort. While adjustments were made for the presence of mesenteric ischemia, the retrospective nature of this study means that accurate data on infective complications were not available. If the patients with elevated CRP had a higher rate of infective complications, this may account for the survival disadvantage observed. The literature reporting infective complications after aneurysm surgery is limited to the elective setting, where infection rates following OSR may approach 7%.[34] Therefore, it may be anticipated that the presence of infection would not be a significant factor in the present results. The thresholds of postoperative CRP and the choice of day 3 CRP used for prognostication in this study lack external validation, which is a potential source of bias. This study reported 72% of patients in the emergency cohort undergoing OSR rather than EVAR as their repair strategy. This is slightly higher than contemporary UK data (60% rAAA OSR rate in 2021 across all UK units),[35] however, is comparable to Scottish national data recorded during the time period of study recruitment. Given the expected difference in physiological insult caused by open or endovascular repair strategies, there is likely to be a difference in postoperative SIR. This study did not include patients undergoing elective EVAR as they were typically discharged prior to the third postoperative day, potentially introducing bias into our results. Future studies could include these patients through measurement of inflammatory parameters in the outpatient/ambulatory setting. The mGPS was originally described in patients with cancer, and despite reports of its prognostic value in cardiovascular disease it remains underreported in these cohorts, which is a potential source of bias. Finally, this study is limited by retrospective study design, missing data for some parameters, and low absolute numbers in certain subgroups.

CONCLUSIONS

Preoperative and postoperative markers of systemic inflammation were independently associated with inferior survival following emergency and elective repair of AAA, respectively. Further investigation of the perioperative SIR is warranted in this patient group, with a particular focus on identifying targets for intervention.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Nicholas A. Bradley: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. **Amy Walter:** Writing – review & editing, Formal analysis, Data curation. **Alasdair Wilson:** Writing – review & editing, Investigation, Data curation. **Tamim Siddiqui:** Writing – review & editing, Investigation, Data curation. **Campbell SD. Roxburgh:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization. **Graeme JK. Guthrie:** Writing – review & editing, Supervision, Project administration, Data curation, Conceptualization. **Donald C. McMillan:** Writing – review & editing, Supervision, Project administration, Investigation, Conceptualization.

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