REVIEW ARTICLE

C-reactive protein and digestive pathologies: A narrative review for daily clinical use

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The aim of this narrative review is to familiarize clinicians, especially digestive surgeons, to adequately use of serum C-reactive protein as a reliable noninvasive biomarker in diverse practical clinical situations. We hope that the review will help clinicians for their decision-making when facing various digestive diseases including operative and nonoperative pathologies such as anastomotic leakage, pancreatitis, emergency situation, and digestive cancer management and prognosis.

Key words: Cancer prognosis, C-reactive protein, digestive surgery, postoperative complications

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INTRODUCTION

C-reactive protein (CRP) is an annular, 206-amino acid, pentameric protein belonging to the pentraxin family. It is synthesized by the liver and present in plasma following the secretion of interleukin-6 (IL-6) by macrophages and T-cells in response to tissue damage or inflammation[1-4] [Figure 1]. The CRP gene is located on chromosome 1.[5] Its physiological role is multiple.[4,6] One of these roles is binding to lysophosphatidylcholine on the surface membranes of dying cells or microbes (such as bacteria) to activate the complement system, opsonization, and phagocytosis.[7] IL-6 secreted mainly by macrophages and/or adipocytes triggers the synthesis of CRP and fibrinogen by the liver as a primary quick response to any inflammation.[4,6]

Other ILs such as tumor necrosis factor (TNF) alpha and transforming growth factor beta-1 can increase serum CRP level.[8] This response to inflammation is non-specific and occurs in various inflammatory conditions, including bacterial, fungal, and viral infections; rheumatism; inflammatory and allergic diseases; certain malignancies; and other forms of tissue damage or necrosis.[9-17] Some recent articles report a relationship possible between CRP, IL-1, IL-6, and depression[18] [Figure 2]. CRP with fibrinogen and procalcitonin (PCT) is the most conventional serum biomarker used in clinical practices, especially among patients with systemic inflammatory responses.[19]

The normal serum level of CRP is <10 mg/L (1 mg/dL). Although some healthy adults have moderately elevated CRP, this is mainly due to gene polymorphism.[20,21] During acute inflammation, CRP can increase from 10 mg/L to 100 mg/L within 4-6 hours, while PIC can increase up to 10,000-fold (more than 500 mg/L). CRP serum concentration can double every 8 h. The peak can

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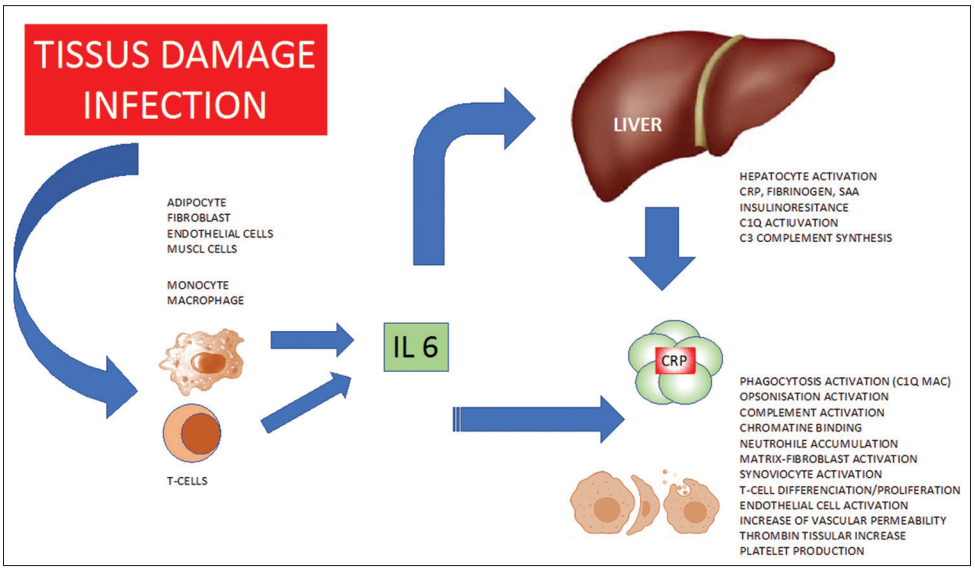

Figure 1: C-reactive protein synthesis by the liver after tissue damage/infection under interleukin-6 secretion and its major peripheral effects. CRP: C-reactive protein, IL 6: Interleukin 6

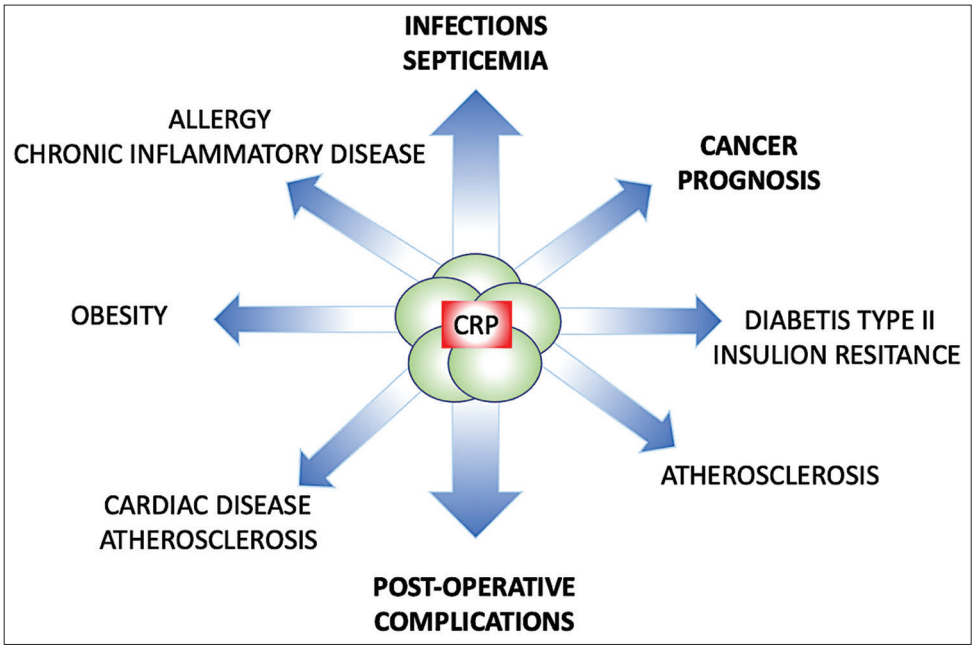

Figure 2: Implication of C-reactive protein in myriad of pathologies. CRP: C-reactive protein

be reached after 36–50 h. Therefore, a serum CRP between 100 and 500 mg/L is highly predictive of acute inflammation, mainly after bacterial infections.[4] Its relatively short half-life (19 h) is a good predictor biomarker of the improvement of global inflammation within a day.[22] CRP is sensitive but not a specific biomarker for infections. Serum CRP can be slightly elevated in some individuals such as newborns, adults under high-protein diet, smoking, aging, pregnancy, obese, insulin-resistant patients (metabolic syndrome), and those with elevated triglycerides. The global scope and postoperative kinetics of CRP in main digestive operations are represented in Figures 2 and 3.

This review reports a practical synthesis of published English articles of the past 10 years on CRP and different digestive pathologies such as cholecystitis, diverticulitis, appendicitis, and pancreatitis. Remarkably, CRP can help clinicians to accurately detect postoperative complications such as anastomotic leakage (AL) and other infective complications.

C-REACTIVE PROTEIN AFTER ABDOMINAL AND PARIETAL SURGERY

The serum CRP level increases after any abdominal surgery.[23] CRP level is higher in patients with any

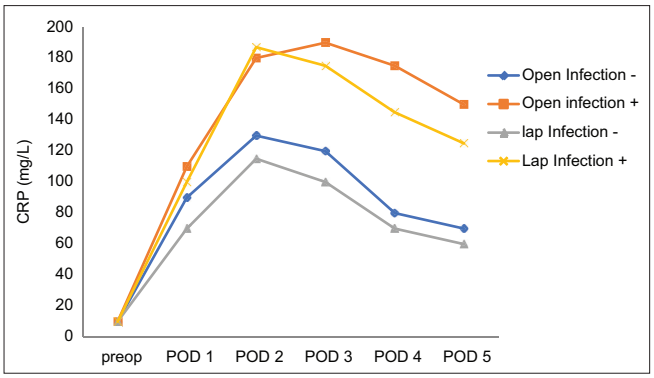

Figure 3: C-reactive protein increase kinetics after postoperative infectious complications of abdominal open and laparoscopic surgeries. CRP: C-reactive protein, POD: Postoperative day, PREOP: Preoperative period

postoperative infectious complications.[24-26] Serum CRP <150 mg/L, on postoperative day (POD) 2–5, is predictive of absence of postoperative infectious complications, whereas a serum CRP level >150 mg/L, even after 36 h of surgery, is a reliable predictive of postoperative infectious complications.[24-26] This remains true for open and laparoscopic digestive surgeries.[24,26] Serum CRP increases in a lower manner in patients without postoperative (PO) infectious complications after laparoscopy versus open surgery. For both open and laparoscopic surgeries, the level of CRP >150 mg/L on POD 2 remains a good predictive marker of PO infectious complications. In these situations, serum CRP had the best diagnostic accuracy for severe infectious complications on POD 6 (area under the curve [AUC]: 0.73) and POD 7 (AUC: 0.63). A serum CRP cutoff of 120 mg/L, on PO 6, had a negative predictive value (NPV) of 96.1%, and a CRP cutoff of 80 mg/L on POD 7 had a NPV of 94.9%.[27] However, in most of digestive surgeries with anastomoses, serum CRP as early as POD 1 seems to be related to occurrence of AL.[26,28]

High CRP level has been reported as a reliable predictive factor of complications after hernia surgery with mesh. Janet *et al*.[29] reported 80% sensitivity and 95.2% specificity for serum CRP cutoff level of 100 mg/L after incisional hernia repair by biological meshes. For this cutoff, complication rate before POD 10 was 95% in the CRP >100 mg/L group versus 46% in the CRP <100 mg/L group. The authors concluded that a high postoperative level of serum CRP may serve as a marker of postoperative complications. For Pochhammer *et al*.,[30] patients with high serum CRP levels at POD 5 and POD 6 may have an increased risk of surgical site complications after ventral hernia repair with various types of synthetic meshes and require closer surveillance. A CRP <105 mg/L on POD 2 or 3 had the highest NPV of 100% and a positive predictive value (PPV) of 29% (sensitivity 100% and specificity 55%). A CRP cut-off of 63 mg/L predicts infectious complications with a sensitivity of 69% and a specificity of 83%, a PPV of 46% and a NPV of 93%.

C-REACTIVE PROTEIN AFTER ESOPHAGECTOMY AND GASTRECTOMY

Aiolfi *et al*.[31] reported that a serum CRP level of >170 mg/L on POD 3 is a reliable predictor biomarker of infectious complications, mainly secondary to AL after esophagectomy, while this cutoff of CRP was >150 mg/L at POD 3 after gastrectomy. Remarkably, the NPV of CRP was an excellent marker of absence of complication, as a low CRP serum level from POD 1 to POD 6 had a NPV ranging from 94% to 100% and from 70% to 100% after esophagectomy and gastrectomy, respectively. On the contrary, the PPV was either not reported in several studies, and when reported, it ranged from 20% to 50% after esophagectomy and from 21% to 83% after gastrectomy, signifying that PPV was poorer than NPV for a relevant clinical use.

In a practical point of view, if a patient presents no clinical symptom such as pain and fever and if the serum CRP level is low after POD 5 or POD 6, the discharge is reasonable even without computed tomography (CT)-scan, while the presence of a low CRP associated with any other worrisome clinical symptom should require oral contrast CT scan, to eliminate AL or other infectious complications such as pulmonary infection.[32-34] For Stuart *et al*.,[35] serum CRP levels of >110 mg/L, on POD 4, have a high sensitivity to exclude AL, allowing discharge of patients. This point was confirmed by Rat *et al*.,[36] who showed that serum CRP had the best PPV value for the detection of AL on POD 5, with a cutoff >130 mg/L (sensitivity of 87%, specificity of 51%, and NPV of 96%). Barbaro *et al*.[33] reported on a systematic review that the value of serum CRP, pleural drain amylase, and CT with oral contrast as simple elements to predict AL after esophagectomy. Serum CRP <145 mg/L on POD 4 seems to be accurately associated with absence of AL after esophagectomy for cancer, as well as low CRP/lymphocyte ratio (CLR) <300.[37,38]

Nomograms including sex, type of anastomosis, reconstruction route, personal history of smoking, cardiac arrythmia, diabetes, and serum CRP were predictive of AL after esophagectomy.[39] In western countries, a serum CRP level <85 mg/L with absence of clinical and radiological worrisome signs seems more accurate to allow early discharge after esophagectomy.[34] Regarding the timing and cutoffs of serum CRP level after esogastrectomy, predictive values change significantly upon timing. For Gordon *et al*.,[40] serum CRP levels on POD 2, 3, and 6 had a great diagnostic accuracy, with an AUC of 0.82, 0.80, and 0.90, respectively. When using CRP >209 mg/L, on POD 2, the sensitivity was 100%, the specificity 61%, the PPV 21%, and the NPV 100%. When using CRP >190 mg/L on POD 3, the sensitivity was 100%, the specificity 59%, the PPV 21%, and the NPV 100%. Using CRP >154 mg/L on POD 6, the sensitivity was

100%, the specificity 78%, the PPV 29%, and the NPV 100%. Therefore, it seems that postesogastrectomy serum CRP measurements are quite accurate as NPV but not as PPV.

Concerning CRP and gastrectomy complications, a serum CRP cutoff <115 mg/L, on POD 3, also seems to be a reliable NPV for absence of AL.[41] CRP levels <217 mg/L, on POD 2, and a CLR of <300 presented excellent NPV of 97% and 98%, respectively.[38] Tanaka *et al*.[42] reported the importance of calculating serum CRP ratio regression per PODs after laparoscopic gastrectomy for cancer. A value of serum CRP ratio on POD 3/POD 1 >2.13 was the best predictor of occurrence of severe complications. Lee *et al*.[43] reported that NPV of patients without postoperative complications was a decrease in serum CRP level of >10% between POD 2 and POD 3 and even between POD 3 and POD 5.

C-REACTIVE PROTEIN AFTER BARIATRIC SURGERY

Bariatric and metabolic surgeries can significantly reduce the inflammatory biomarkers such as CRP, IL-6, and TNF-α.[44,45] One year after bariatric surgery, when the mean weight loss was 32.5% ±8%, serum CRP decreased from 9.0 (3.7–13) to 1.1 (0.3–3) mg/mL ($P < 0.001$), while fibrinogen decreased from 4 ± 8 to 3.5 ± 8 g/L ($P < 0.001$).[46] Lee *et al*. [47] reported a meta-analysis including 2770 patients from six studies concerning CRP and postoperative infectious complications after bariatric surgery. Serum CRP cutoff values of 71 mg/L, 130 mg/L, and 119 mg/L on PODs 1, 3, and 5 were significantly correlated to the presence of infectious complications. The PPV ranged from 19% to 21% and the NPV from 98% to 99%. Serum CRP levels on both PODs 3 and 5 were significantly higher in patients with postoperative infectious complications versus those without. Bona *et al*.[48] reported another meta-analysis including seven studies for a total of 1401 patients who underwent bariatric surgery. Sensitivity and specificity of CRP values among complicated patients on POD 1 with a cutoff of 61 mg/L were 82% and 92%, respectively. Whereas, on POD 2, a CRP cutoff of 154 mg/L, represent a sensitivity and specificity of 84% and 78%, respectively. In Yang *et al*.[49] meta-analyses, serum CRP had a relatively good diagnostic accuracy for the prediction of postoperative complications. The sensitivity and specificity for AL after bariatric surgery were 81% (34%–100%) and 91% (73%–100%), respectively, while this was 95% (75%–99%) and 95% (75%–99%), after colorectal (CR) surgery. Bona *et al*.[48] suggested to consider no complication on POD 1 when serum CRP was <60 mg/L on POD 1 without any worrisome clinical sign (including tachycardia). In a retrospective cohort including 587 patients, CRP values on POD 1 and POD 3 were compared between patients presenting major (n = 14, 10 cases of AL) or no major complications. The cutoff value of CRP on POD 3, for diagnosis of AL, was 147 mg/L with 56% sensitivity and 87% specificity.[50] This was close to cutoff serum CRP levels of 150 mg/L reported for detection of AL after gastrectomy for cancer (see chapter above).

C-REACTIVE PROTEIN AFTER COLORECTAL SURGERY

Two reviews and meta-analyses are available.[26,28] Yeung *et al*.[28] reported a systematic review and meta-analysis concerning CRP for occurrence of AL in CR surgery and included 23 comparative studies and 6647 patients of whom 482 (7.2%) had AL. High CRP levels were observed in patients with AL on POD 1 up to POD 7. For these authors, a serum CRP cutoff level of 180 mg/L, on POD 2, can accurately predict AL for CR surgery. Remarkably, a serum CRP level >148 mg/L on POD 3 had a sensitivity and specificity of 95% for AL occurrence, while serum CRP levels >123 mg/L on POD 4, >115 mg/L on POD 5, >105 mg/L POD 6, and >96 mg/L on POD 7 had almost a sensitivity and specificity of 100%.

The comparison between open and laparoscopy revealed two other cutoff values.[26] A serum CRP level >170 mg/L, on POD 3 (after open), and >150 mg/L (after laparoscopy) were associated with a PPV ranging from 59% to 70%, while NPV values ranged from 62% to 70%. These points mean that reported cutoff values cannot predict all of AL from POD 3 to POD 5 alone and highlight the importance of other factors such as clinical symptoms and/or amylase level in the drainage liquid if available.[51] For patients undergoing CR surgery and cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC), a lower cutoff value of serum CRP >90 mg/L on POD 5 was reported to be related to the presence of postoperative infectious complications with a sensitivity of 79%, a specificity of 76%, a PPV of 63% and a NPV of 87%.[52] For Welsch *et al*.,[53] a cutoff level of serum CRP >140 mg/L after POD 3 is a reliable biomarker of infectious complications after CR surgery. For Almeida *et al*.,[23] the same cutoff values of CRP on POD 3 had a sensitivity of 78% and specificity of 86% to predict occurrence of AL. For Ortega-Deballon *et al*.,[54] a serum CRP <125 mg/L on POD4 can safely let discharge the patients from the hospital. When the serum CRP level is higher than reported and/or when serum CRP levels stagnate on POD, even in the absence of clinical worrisome signs, a CT scan can help clinicians to manage patients.[55] For Holl *et al*.,[2] a serum CRP level on POD 4 >125 mg/L should indicate CT scan. In conclusion, for CR surgery, a cutoff of serum CRP level >150 mg/L, on POD 3/4, seems to be a reliable factor for initiate the detection of postoperative complication including AL.[56,57] Interestingly, some data show that preoperative administration of corticosteroids (dexamethasone) can reduce the magnitude of postoperative inflammatory response and reduce complications after CR surgery.[58,59]

C-REACTIVE PROTEIN AND PANCREAS PATHOLOGIES

C-reactive protein after acute pancreatitis

Digestive surgeons are faced to give therapeutic opinion in patients with severe acute pancreatitis. This small chapter reports some important points concerning CRP and acute pancreatitis.

CRP has no value as compared to serum lipase level (>3-fold N), for diagnosis of acute pancreatitis.[60,61] However, it has been historically used, after 48 h admission, in patients presenting severe acute pancreatitis, to predict infectious complications.[62-66] A CRP level >140 mg/L, from hospital admission day 3, in patients with pancreatic necrosis (or collections), accurately predicts infectious complications requiring function and/or drainage of such collections, especially when bubbles are detected in CT scan.[60,65-68] This includes bacterial as well as fungal infections.[69-72] Greenberg *et al*.[73] reported that a serum CRP > 150 mg/L within the first 72 h of admission in patients with acute pancreatitis is associated with a worse clinical course. However, other series have reported a low PPV of this cut-off, while the NPV appears to be accurate.[74,75]

Chen *et al*.[76] reported four factors (hematocrit, urea, CRP, and PCT) as independent for the diagnosis of pancreatic necrosis infection within 48 h of admission. When these four factors were combinedly, it could accurately predict infected pancreatic necrosis with a sensitivity of 68% and a specificity of 77%. Other serum biomarkers such as CD64, lactate dehydrogenase, and PCT seem to be interesting to predict bacterial infections in patients with severe pancreatitis.[77] Recent articles showed that CRP/albumin ratio had a higher sensitivity and NPV than CRP alone giving additional advantages as a prognostic biomarker in patients with severe pancreatitis.[78]

C-reactive protein after pancreatectomy

After pancreatoduodenectomy (PD) and/or distal (left) pancreatectomy, the drain amylase level, as soon as POD 1,[79] predicts occurrence of postoperative pancreatic fistula (POPF).[69,80-84] In addition, the occurrence of clinically relevant POPF remains the main factor that significantly increases the postoperative morbidity and mortality rates.[80] Together with other signs, serum CRP level and its kinetics could help to predict clinically relevant patients with POPF.[85-88] Guilbaud *et al*.[89] grouped low drain amylase level (<1000 UI/L) and low serum CRP (<90 mg/L) as soon as POD 1 and reported a PPV of 74% and a NPV of 74% for diagnosis of clinically relevant POPF. A CRP level >140 mg/L, on POD 3, seems to be sensitive enough to predict clinically relevant POPF after pancreatectomy (PD as well as distal pancreatectomy).[88,90-92] Hiyoshi *et al*.[92] reported a cutoff of CRP >200 mg/L, with an excellent AUC of 0.957 (sensitivity 85% and specificity 98%). Fukada *et al*.[93] reported a cutoff of serum CRP >200 mg/L as a reliable PPV for occurrence of POPF. Iwasaki *et al*.[90] showed that a drain amylase level <350 UI/L together with a serum CRP level <140 mg/L on POD 3 could accurately predict absence of clinically relevant POPF. They reported the incident of clinically relevant POPF of 6%, 38%, and 88% in patients who fulfilled both, each of, and none of two factors, respectively.

Vilhav *et al*.[94] reported that serum CRP >180 mg/L on POD 2–3 (univariate), and CRP >140 mg/L on POD 4–5 (multivariate analyses) as significant risk factors of postpancreatectomy hemorrhage. For Uchida *et al*.,[95] the presence of vascular abnormally on early postoperative CT scan and a high serum CRP level, both on POD 3, are risk factors of occurrence of postoperative hemorrhage after PD. When combining serum CRP and derived neutrophil–lymphocyte ratio (dNLR), PPV increased to 67%, and NLR >1.65 was significantly associated with postoperative hemorrhage after PD.[96] For Hiyoshi *et al*.,[92] the absence of clinical signs, low drain amylase, and a serum CRP level <20 mg/L on POD 5 could safely allow drain removal after PD. For Mintziras *et al*.,[79] a high drain amylase and a serum CRP level >200 mg/L were in multivariate analyses, independent predictor factors of occurrence of clinically relevant POPF after PD.

Li *et al*.[84] proposed a simple nomogram predicting the percentage of occurrence of clinically relevant POPF between POD 1 and POD 3 including factors such as drain amylase (POD 1), serum creatinine (POD 1), serum CRP level (on POD 1), neutrophil count (POD 3), and patient temperature (POD 3) after pancreatectomy. Giardino *et al*.[97] reporter a higher risk of clinically relevant POPF after PD in patients presenting on POD 1 a serum CRP >92 mg/L and PCT >0.4 mg/dL. In Chen *et al*.'s[98] meta-analysis, a serum CRP level >150 mg/L on POD 4 and a PCT >0.5 mg/dL on POD 5 were valuable biomarkers to predict occurrence of clinically relevant POPF. For laparoscopic PD, both CRP and PCT on POD 2, 5, and 7 were predictors of clinically relevant POPF.[99] In a review article, Vasavada and Patel[100] showed that serum PCT levels on POD 3 seem to be a better marker, rather than serum CRP on POD 3, for the detection of infectious complications after pancreatic surgery; however, no prospective study yet compared these biomarkers. For Juez *et al*.,[91] the drain amylase level at POD 5 was the best predictor factor for POPF after distal pancreatectomy. They reported other factors such as preoperative body mass index and serum CRP level at POD 3, as predictor of clinically relevant POPF, while CRP >190 mg/L was the best cutoff point (sensitivity 89% and specificity 67%). In addition, associating drain amylase and serum CRP seems to be

interesting tools to predict clinically relevant POPF after distal pancreatectomy (drain amylase POD 2 >1500 UI/L, high serum amylase/lipase levels at POD 1, and serum CRP levels increase of >25 mg/L on POD 3).[101,102] Chen *et al*.[103] reported that both serum lipase on POD 1 and serum CRP level on POD 3, as being reliable predictors of clinically relevant POPF. This point was reported in two articles by Bannone *et al*.[104,105] emphasizing higher morbidity rate after PD in such patients.

Notably, assessment of preoperative systemic inflammatory biomarkers such as NLR or dNLR and serum CRP levels has been reported to predict complications after PD.[96] Patients with CRP before surgery >88 mg/L were at higher risk of overall complications including intra-abdominal collections with a PPV of 95%, NPV of 27%, PPV of 59%, and NPV of 68%, respectively.[96]

C-REACTIVE PROTEIN AFTER HEPATOBILIARY SURGERY

As the liver produces serum CRP under IL-6 stimulus, the levels of serum CRP after hepatic resection (HR) are more complex to study. de Jong *et al*.[106] reported the first clinical data about kinetics of postoperative CRP following HR for CR liver metastases (CRLM) and showed an increase of serum CRP levels on POD 1 with a tendency to a decrease toward normal values on POD 4 in uncomplicated patients. For Rahman *et al*.,[107] a low serum CRP increase on POD 1 and the extent of HR were independent predictors of postoperative liver failure. In fact, some scores included CRP as marker of postoperative liver failure. Among them, the 3–60 criteria on POD 1 (with CRP <3 mg/dL and ATIII <60%) were found to be significantly correlated to postoperative liver failure and an being an independent predictor of occurrence of postoperative mortality after HR.[108]

Postoperative serum CRP levels were also associated with the presence of septic complications after HR. The Heidelberg group[109] reported the postoperative serum CRP in 451 patients who undergone minor and 384 patients major HRs. Serum CRP levels had less PPV after major HR rather than minor HR. Furthermore, serum CRP levels were significantly increased on POD 5 and POD 7, exclusively in patients with minor resections and complications, particularly those who experienced bile leakage.[109] Recently, Pattou *et al*.[110] reported a preliminary multicenter study of 500 h in three French hepatic centers. The study was retrospective and included 36.3% major open HR, 50.6% laparoscopic HR, and 4.4% HR with bilioenteral reconstructions. The rate of bile leakage was 12.4% with a mean diagnosis delay of 8.6 ± 9 days. The mean serum CRP, on POD 1 and 3, was significantly higher in patients with biliary leakage versus those without (76.4 vs. 43 mg/L and 144 vs. 95 mg/L, $P = 0.001$), respectively. A serum CRP level <100 mg/L on POD 3 had a NPV of 93% (sensitivity 67%, specificity 62%, and PPV 13%) for occurrence of biliary leakage. The serum POD 3 CRP was not correlated to the seriousness or treatment modality of the biliary leakage. Fujiwara *et al*.[111] reported the Glasgow Prognostic Score (GPS) (based on preoperative CRP) and showed that high GPSs were associated with higher rate of blood transfusion and pulmonary morbidity after elective HR in patients presenting hepatocellular carcinoma (HCC).

PCT and CRP are showed to be reliable biomarkers of occurrence of infectious complications after total hepatectomy and liver transplantation.[112] In this regard, and particularly after HR, PCT rather than CRP seems more accurately to predict the occurrence of postoperative outcome. PCT on POD 2 <0.35 ng/ml was associated with better outcome regardless of the type of HR. In addition, preoperative steroid administration before HR was reported to reduce postoperative bilirubin and biomarker of inflammation such as CRP and decrease the morbidity rate.[113]

C-REACTIVE PROTEIN AND ACUTE ABDOMINAL INFECTIOUS DISEASES

Acute appendicitis

Acute appendicitis (AA) is the most communal causes of acute abdomen.[114,115] The diagnosis of complicated AA is crucial in both pediatric and adult patients.[116] Many scores have been proposed for the AA diagnosis.[117] However, the ALVARO and RIPASA are mainly diagnostic scores and do not include CRP (mainly clinical scores).[118] Prediction models based on presence of fever, serum CRP level, presence of intra-abdominal collection, and US-appendix diameter have been used to define "high-risk" patients. Atema *et al*.[119] established that the use of scoring systems (combining clinical and imaging signs) can accurately diagnose 95% of the uncomplicated AA. Di Saverio *et al*.[117] reported in 2020 an update of previous guidelines.

NPV are biomarkers such as CRP that have been demonstrated reducing the dependence of CT scan evaluation in many patients; however, slight change of CRP had a modest diagnostic value. A combination of serum biomarkers and US or CT scan may significantly improve AA diagnosis in both adults and children.[114] White blood cell (WBC), CRP, and PCT have been used for diagnosis of AA. Zouari *et al*.[120] showed that CRP >10 mg/L was a good predictor of AA in young children (<6 years old). Yu *et al*.[121] showed lower accuracy for serum PCT. For Blok *et al*.,[122] a CRP <10 mg/L should be interpreted upon presence or absence of clinical symptoms. For some authors, serum

CRP and WBC are the best predictor of positive diagnosis of AA in children.[123]

Anyhow, the performance of US, CT scan, and even magnetic resonance imaging (especially in pregnant women) become routinely performed after initial assessment and risk stratification using clinical and biological scores.[124] Furthermore, when a nonoperative management of AA is retained, a careful patient selection after clinical, biological, and imaging assessment is required. Usually, patients with gangrenous, abscess, and peritonitis are excluded. A serum CRP level <60 g/L, WBC <12,000/mm^3, and an age <60 years old had a chance of 89% of recovery after antibiotic treatment without surgery.[125] The presence of appendicolith has been reported as a factor of failure of medical treatment of AA.[117,126-128] Kubota *et al*.[129] reported the efficacy of nonsurgical therapy in patients with small appendicoliths (<5 mm in diameter) and when serum CRP was <50 mg/L. In a recent multicenter randomized controlled trial (RCT), Puputti *et al*.[130] reported the APPSYPP trial modalities to randomize patients to receive emergency laparoscopic appendectomy versus medical treatment. Criteria for inclusion are (i) age >7 and <16 years old, (ii) imaging confirming uncomplicated appendicitis, and (iii) serum CRP <65 mg/L, while in some other RCTs such as APPACIII trial, no cutoff for CRP has been mentioned in both groups.[131,132] Recent ATOMS RC trial for the management of AA during pregnancy[133] suggests using a predictive score including the CRP/platelet ratio. For Yuksel *et al*.,[134] the most specific biomarkers to predict perforation in patients with AA were CRP/albumin (87.8%) ratio, followed by CRP (85.7%), monocyte/lymphocyte ratio (>0.44), and appendiceal diameter >9.8 mm. At admission, serum CRP/albumin ratio seems to be a promising biomarker to predict and differentiate complicated from noncomplicated AA.[135]

In a recent study, Di Mitri *et al*.[136] reported the important role of combining IL-6 to CRP for the diagnosis of early-stage AA. For Frongia *et al*. and others,[137,138] appendectomy can be delayed around 9 h in children with slight appendiceal perforation without increasing morbidity under certain conditions.

Acute cholecystitis

CRP and WBC have been historically used in parallel of clinical and imaging for the diagnosis of acute cholecystitis AC.[139] CRP serum level decrease has been reported to be related significantly to the success of medical management of AC Grade 2 and 3.[140] In this study, patients were divided into two groups. Group 1 included responders to medical treatment in <3 days and discharged before day 3, and Group 2 included nonresponders who stayed >3 days at hospital. The mean age (51 ± 16 vs. 59 ± 15; $P = 0.013$), total leukocyte count (12 ± 4 vs. 8 ± 2; $P = 0.0005$), and CR*P* value (193 ± 139 vs. 96 ± 52; $P = 0.0003$) were higher in Group 2 versus Group 1. Bivariate analyses found a positive significant association between hospital stay, leukocyte count ($r = 0.35$; $P = 0.0002$), and CRP value ($r = 0.59$; $P = 0.0004$). Several studies showed CRP levels association with AC as predictive factor for the assessment of severity and effectiveness of the medical treatments.[141,142] Mok *et al*.[141] reported that patients with gangrenous cholecystitis had higher CRP level. With a cut-off CRP level of 200 mg/dL, the PPV and NPV were 50%, 100%, respectively, with a sensitivity of 100% and a specificity of 87.9%. Nikfarjam *et al*.[143] reported that a CRP level greater than 94 mg/L was predictive of gangrenous cholecystitis. Sato *et al*.[144] reported that serum NLR and CRP/albumin ratio as reliable for diagnosis of Grade 2 and Grade 3 AC. In addition, for Kabul Gurbulak *et al*.,[145] CRP level was a robust predictor marker for classifying different grades of AC (Tokyo Guidelines [TG] 13). CRP >70 mg/L had 75% sensitivity and 97% specificity in patients with Grade 2 AC and CRP >190 mg/L with 74% sensitivity and 76% specificity in patients with Grade 3 AC. Several other articles associated CRP, WBC, and NLR as reliable predictors of the severity of AC.[146,147] Mahmood *et al*.[148] found that patient's age (odds ratio [OR] = 1.047; $P = 0.003$), CRP level (OR = 1.005; $P = 0.012$), and NLR (OR = 1.094; $P = 0.047$) as reliable predictors for AC severity.

For Bouassida *et al*.,[149] CRP was the best biomarker predicting the severity of AC and the risk of conversion of laparoscopy to open. In addition to TG13,[150] the duration of symptoms >72 h and CRP serum level were independent risk factors for conversion of laparoscopy to open surgery for AC Grade 2. In TG18,[151] the flowchart for the management of AC does not include the value of any biomarkers. For Grade 1 AC (mild), laparoscopic cholecystectomy is recommended as soon as possible unless patient cannot withstand surgery. For Grade 2 AC (moderate), laparoscopic cholecystectomy is recommended in specialized centers; if not, conservative treatment (with or without drainage) is recommended. For Grade 3 AC (severe), early surgery is only recommended by a specialized surgeon, and if the general condition of the patients allows surgery and hospitalization in ICU, otherwise conservative management should be performed in all patients, and biliary drainage is indicated, if AC is not controlled by medical treatment. In TG18, CRP and other biomarkers are used as diagnostic tool but not for severity assessment of AC.[152] For example, in TG13 and TG18, the severity assessment for Grade 2 acute cholangitis includes any of two following biological signs: WBC >12,000 or <4000/mm^3, fever ≥39°C, hyperbilirubinemia ≥5 mg/dl, and hypoalbuminemia (<STD × 0.7).

Considering the risk of bile duct injury, Onoe *et al*.[153] suggested to use preoperative CRP >55 g/L, gallstone

impaction and symptoms starting more than 72 hours before surgery to achieve the critical view of safety in patients undergoing emergency laparoscopic cholecystectomy. Perforated AC represents the most severe type of AC with high rate of morbidity, mortality, and bile duct injury. Jansen *et al*.[154] suggested to use CRP >200 mg/L, especially in >65 years old patients for perforation of diverticulitis. Chen *et al*.[155] reported the value of noninjected CT combined to serum biomarkers that did not include CRP, as a reliable tool for the positive diagnosis of suppurative AC, especially in patients who could not have intravenous injection. In this series, the presence of gallbladder and/or common bile duct stones, gallbladder thickness, and neutrophil count could predict risk factors of suppurative AC and allow to perform percutaneous drainage.

Although percutaneous drainage remains an important therapeutic tool in patients with Grade 2 and 3 AC, the clamping and the removal timing of the drainage catheter and importance of normalization of serum biomarkers are not yet well standardized.[156] Decrease in serum CRP and WBC are usually obtained after 2–3 days of drainage, indicating the decrease in gallbladder wall inflammation Allowing to clamp the external bile drain. However, after its removal, especially in presence of gallbladder stones, there is more risk of symptom recurrence.[156] In patients with AC Grade 2 or more, late cholecystectomy after percutaneous drainage versus early cholecystectomy seems to be associated with shorter surgery time, lower conversion rate, and less intraoperative blood loss.[157,158]

Occlusion, intestinal ischemia, and intestinal perforation

Intestinal obstruction is an acute surgical disease with high risk of morbidity and mortality worldwide.[159] The most important point for surgeons is to propose emergency operation, especially in patients with clinical, biological and/or imaging "worry-some" signs.[55,160] This includes abdominal defense or contracture, fever, hemodynamic instability, renal failure, and CT findings such as thickening intestinal wall, local or diffuse pneumatosis, mesenteric edema, intra-abdominal fluid, and/or bubbles and pneumoperitoneum and exceptionally "Aero Portia".[161] For many authors, serum CRP level of 50 mg/L should be a worrisome sign and CRP >150 mg/L a sign of potential intestinal necrosis and/or peritonitis.[162,163] However, a CRP/albumin >1.32 is reported to have a sensitivity of 94% and a specificity of 70% for intestinal ischemia.[55,164] Neutrophil number, serum L-lactates, neutrophil/lymphocyte ratio, or platelet/lymphocyte ratio do not appear to have good prognostic value, or they may have prognostic value at a later stage in this context.[165] PCT was reported to be a reliable biomarker in patients with intestinal occlusion.[166,167] The recently used endothelin-1, which is a vasoconstrictive peptide derived from vascular endothelium, represents an interesting biomarker for ischemic damage severity and can be used associated with serum CRP in daily practice of clinicians for bowel ischemia and necrosis.[168,169]

Other than serum CRP, PCT, serum urea, lactates, and their ratio to serum albumin seems correctly predict occurrence of complications and mortality.[170] In this publication, the PCT >0.65 μg/L predicted mortality rate of intestinal occlusions, with a sensitivity of 93% and a specificity of 78%. Sabbagh *et al*.[171] reported an algorithm for the management of patients with uncomplicated adhesion-related small bowel obstructions in a multicenter randomized trial. For them, if serum PCT level at admission <0.2 μg/L, a conservative management can be proposed; if serum PCT >0.6 μg/L, surgical management is proposed. For patients with levels in between, a second assessment 24 hours later is advised. If the serum PCT increases by >0.25 μg/L, surgical management should be performed. Intraoperatively, in some patients, especially those with elevated preoperative biomarkers and comorbidities, intraoperative Doppler, fluorescein, and ICG test might present an interest.[172]

As expected, in children (70% male) presenting symptomatic Meckel's diverticulum, those with hemorrhage (with or without heterotopia mostly gastric) presented with anemia, low serum CRP, and a distance to ileocecal valve >40 cm, while those with diverticulitis and occlusion presented with high CRP level and no anemia.[173,174]

Postoperative ileus remains a clinical and economic impact after CR surgery. It appears that postoperative ileus may increase serum CRP level from POD1 to 4, even in patients without postoperative complications such as AL. Furthermore, in such patients, serum levels of some cytokines such as IL-6, IL-8, and IL-10 were significantly increased after the first 2 days after resection in patients who did present postoperative ileus.[175]

Acute diverticulitis or sigmoid perforation

The colonic diverticulosis colon increases with age (50% above the age of 60 years old); however, only 20% of patients might require treatment during their lifetime.[176,177] The most serious complication of diverticulitis remains perforation (10%), especially in immunosuppressed patients.[55] Even if early stages of diverticulitis are nowadays treated without antibiotics,[178] early detection of perforation in at-risk patients and those who failed after nonoperative treatment remains a challenging goal for clinicians to reduce morbidity and mortality rates.[179] Serum CRP has been largely used for diagnosis and severity of diverticulitis in concert with clinical and imaging tools.[55] In this regard, CRP with fever, increased WBC, and presence or absence of vomiting are secondary diagnostic criteria on the initial evaluation, while abdomen rigidity, hypotension,

elevated serum lactates, and patient performance remain among main initial and severity diagnostic criteria.[180] Guidelines with various classifications (Hinchey I, II, III, IV or qSOFA) are available to guide the proper management of the disease.[55,181] Mannheim Peritonitis Index accurately reports the morbidity and mortality rates in patients with perforated diverticulitis and peritonitis.[182] Comorbidities remain an important risk factor of mortality in combination with intra-abdominal signs of peritonitis such as free fluid on CT.[181,183]

Concerning serum CRP and uncomplicated diverticulitis, Azhar *et al*.[178] recently reported the two different hospitals in Sweden, one with and the other without antibiotic protocol. The study included 583 patients with uncomplicated acute diverticulitis (195 treated with antibiotics and 388 without antibiotics). Diagnosis was assessed with CT scan in 186 (95%) and 320 (83%) patients , respectively. Forty-three (11%) and 94 (48%) of patients did not receive antibiotics during hospitalization ($P < 0.001$), respectively. CRP was higher in the antibiotic group versus nonantibiotic group (90 mg/L vs. 65 mg/L; $P = 0.016$ and 138 mg/L and 97 mg/L; $P < 0.001$), for both admission and peak levels, respectively. There were no significant differences in terms of recurrences (22% vs. 22%; $P = 0.87$), complications (2.5% vs. 2.9%; $P = 0.77$), or hospital stay (3 days of median) between the antibiotic/nonantibiotic groups. The study was retrospective; the difference between CRP in antibiotic versus no-antibiotic patients is therefore comprehensive. However, multivariate analyses at admission for acute uncomplicated diverticulitis patients with elevated CRP and presence of hospital protocol were identified as the two independent risk factors for administration of antibiotics. Bolkenstein *et al*. reported elevated serum CRP level as a risk factor for failure of nonantibiotic management of uncomplicated acute diverticulitis.[184,185]

CRP kinetics has been used to decide whether a patient who is under nonoperative management should be operated. Ahmadi *et al*.[186] classified patients in low, rapid, and high-rise groups of CRP during 48 h of admission and found a correlation for the need for intervention. This reinforces Mäkelä *et al*.[183] and Kechagias *et al*.,[187] suggesting serum CRP >150 mg/L as being predictive of complication. Mäkelä *et al*.[183] also added to this cutoff, old age as additional risk factors to predict severity of acute diverticulitis even at patient hospital admission (sensitivity 85% and specificity 65%, AUC of 0.811, $P = 0.0001$). According to Jaung *et al*., [188] factors associated with worse outcomes in patients with CT-confirmed uncomplicated acute diverticulitis include a high pain score, initial systemic inflammatory response syndrome, elevated CRP, the first episode of diverticulitis, and chronic use of immunosuppressants. Selecting patient for nonantibiotic management might, in our opinion, take into account age (> or <70 yo), presence of comorbidities, and serum CRP >170 mg/L as higher risk factors for nonantibiotic failure of uncomplicated diverticulitis as partly suggested by Bolkenstein *et al*.[184] As reported,[189] initial high serum CRP level, with or without antibiotics treatment, represents an independent predictor factor for medical treatment failure, suggesting to reperform a CT scan if the patient had no decrease in CRP level after 48 h. However, the presence of isolated pericolic bubbles in a patient with favorable clinical and biological indicators can be suitable for nonantibiotic treatment.[189,190]

Curiously, there was no recent reported article concerning regression kinetics of CRP after nonoperative management of complicated diverticulitis, especially in patients who required radiologic drainage of abscess larger than 3 cm (modified Hinchey IB and II), nor after drainage and before ablation of percutaneous drain, especially in immunosuppressed patients.[55,180,191]

C-REACTIVE PROTEIN AND CANCER PROGNOSIS

Tumor microenvironment plays and important role in cancer development, progression, and metastasis.[192] Inflammatory responses in tumor microenvironment can be measured by unspecific biomarkers, especially cytokines, leukocytes, and other subtypes.[193-195] Different biomarker values can reflect this dynamic balance of the immune system.[196] Inflammatory cells such as macrophages, themselves activated by tumor cells, and environmental damages can play tumor promoter role by creating inflammatory matrix, that is, a facetious environment for tumor growth, DNA damage, angiogenesis, and tumor spread and metastasis.[197,198]

In this regard, pretreatment elevation of serum CRP could indicate tumor aggressiveness reflecting indirectly a poorer prognosis.[199,200] Interestingly, it was reported that even slight elevation of CRP is associated with higher risk of overall cancer.[199] The reported studies included demographic characteristics (age, gender, and performance status), tumor characteristics (histology and site), tumor stage (TNM or Dukes), and tumor bioindicators such as carcinoembryonic antigen (CEA), cancer antigen 19-9. However, the reported cutoff values of CRP did not let specific analyses as they ranged from normal (<1 mg/L) to >150 mg/L.[201]

In locally advanced esophageal and rectal cancers, for which a neoadjuvant chemotherapy or chemoradiotherapy is indicated, even slight elevation of serum CRP level, varying from 3 to 10 mg/L, was associated with lesser response rates.[202] In CR, gastroesophageal, pancreatic cancers, and hepatocellular carcinoma, preoperative CRP

was an independent predictor biomarker of RFS and/or overall survivals (OS) after curative surgery with cutoff values varying from 2 to 150 mg/L; nevertheless, in most of studies, the serum CRP cutoff value predicting a poor prognosis was > 10 mg/L.

Some theories can emerge. First, tumor growth can cause inflammation and increase CRP level.[203] Second, some cancer cells express CRP and secrete IL-6 and IL-8 that stimulate liver CRP production.[203,204] Finally, CRP may reflect the host tumor immune response.[203] In addition, some evidence suggest probable role of chronic inflammation in the genesis of malignancies.[204,205] CR and pancreatic cancers seem associated with both local and systemic chronic inflammation and this is from genesis to progression.[206,207] Some tumors are associated with clinical and CT-sarcopenia, which may increase systemic chronic inflammation.[208]

Regarding preoperative CRP and postoperative morbidity in cancer patients, several studies have reported different cutoffs of CRP/albumin ratio (esophageal ≥0.0139,[209] gastric >0.058,[210] and CR CRP ≥17.5 mg/L[211]). In the same manner, Wang *et al*.[212] reported CRP-albumin-lymphocyte index as a reliable biomarker after surgery for poor prognostic patients with epithelial ovarian cancer.

Even if the exact explanation underlying the association between preoperative inflammation and occurrence of postoperative morbidity remains unclear, improving preoperative systemic inflammation might represent a new strategy to decrease postoperative morbidity.[58,59] The anti-inflammatory effect of immune-nutrition may partly explain its benefit in reducing the risk of postoperative infectious complications.[213-215] Furthermore, preoperative administration of corticosteroids significantly reduces preoperative inflammation (CRP) reducing postoperative morbidity.[59,216] Bert *et al*.[217] demonstrated that preoperative serum CRP cutoff level >5 mg/L with a HR = 2.3 (1.3–4.3) was obviously related to worse disease-free and OS after colorectal cancer (CRC) surgery.

GPS combing serum CRP and albumin reflects systemic inflammatory response in different cancer patients including digestive neuroendocrine tumors.[218-222] In pancreatic cancers, GPS = 2 (which correspond to serum CRP >1 mg/L and albumin <3.5 g/dl) showed to be superior to other inflammatory biomarkers in terms of separating good and poor prognostic patients.[223] Moreover, serum CRP decreasing into <3 mg/L during neoadjuvant chemotherapy was associated with better survival than patients with serum CRP >3 mg/L.[224] In gastric cancers, CRP-to-albumin ratio (CAR) >0.1 was reported to be an important prognostic value in predicting the 1-, 3-, and 5-year survivals (1.94 [1.67–2.27]).[225] In esophageal cancer, the survival was significantly higher when the preoperative serum CRP was < 1.5 mg/L versus ≥1.5 mg/L (P = 0.009).[226] The modified GPS has also been proposed for prognostication in patients undergoing surgery for resectable as well as unresectable malignant biliary obstructions.[227] In this regard, we believe that in patients with increased serum CRP level before neoadjuvant treatment or upfront surgery, the serum CRP assessment together with systemic markers such as CEA and carbohydrate antigen (CA)19-9, chromogranin A, after treatment might confirm efficacy or not of such treatments. Recently, Maurer *et al*.[228] reported normal serum CRP, age >60 years old, absence of diarrhea, liver metastatic burden <50%, and treatment with peptide receptor radionuclide therapy (radionucleotide treatments) as independent multivariate good prognostic factors in patients with stage IV small intestine neuroendocrine neoplasms. Matsunaga *et al*.[229] reported in multivariate analysis that CRP/prealbumin ratio but not CRP/albumin ratio, as independent prognostic factor along with lymph node metastasis for patients who underwent esophagectomy for cancer. For Lu *et al*.,[230] both high preoperative CRP and high postoperative CRP level (pic) were associated with worse prognosis in patients with gastric cancer. In addition, after radical gastrectomy, adjuvant chemotherapy seemed to only improve the prognosis of stage I/II gastric cancer patients, exclusively in those with pre-CRP >3.1 mg/L and post-CRP (pic) >77 mg/L.

Many series showed a relationship between high serum CRP levels and worse prognosis of stage III CRC including higher rate of recurrence.[217,222,231-234] Eren[219] reported that lymphocyte-to-CRP ratio (LCR) had the highest impact on predicting survival after curative resection for stage III CRC. In addition to preoperative elevated serum CRP, the presence of anemia and hypoalbuminemia (poor nutrition index) was associated with poorer OS rates after curative intent surgery for stage I to III CRC.[235,236]

Utsumi *et al*.[237] showed that LCR might accurately predict prognosis after liver resection for CRLM. Other series showed the same trend for biomarkers including CEA, CA19-9, and CRP as being related to patient's prognosis after resection of CRLM.[238] Frühling *et al*.[239] reported a composite score including advanced age, raised serum CRP level, hypoalbuminemia, extent of HR, number of metastases, and midgut origin of the primary as being associated with poorer prognosis in patients with CRLM after resection. Deng *et al*.[240] showed that CAR was an independent predictor of OS and recurrence-free survival in patients with CRLM who underwent curative resection. van Dijk *et al*.[241] suggested in patients with CRLM that L3-sarcopenia and/or low visceral fat were not directly associated with systemic inflammation (serum CRP). However, when systemic inflammation coincides with

sarcopenia and/or low visceral adipose tissue (VAT), prognosis was adversely affected, independent of the Fong clinical prognostic score.[242] Interestingly, serum CRP increase was more common in patients with sarcopenia (74% vs. 51%, $P = 0.029$). The most significant prognostic factors were elevated CRP and hostile body composition features (sarcopenia and/or low VAT).

Matsumoto *et al*.[243] reported that CAR was the best independent prognostic factor in patients with HCC. This was also reported after resection in patients with extrahepatic cholangiocarcinoma.[244] Zhang *et al*.[245] reported that preoperative LCR is an interesting biomarker for predicting posttreatment of patients with HCC independently from liver function, tumor characteristics, and treatment allocation. Other series seems to confirm these data.[246] The same biomarker seems to predict the prognosis of patients with intrahepatic cholangiocarcinoma as well.[247,248] Serum CRP level could be an indicator of immunosuppression of tumor microenvironment.[249]

CONCLUSIONS

CRP alone or associated with other biomarkers such as PCT can help clinicians to accurately predict the presence or absence of infectious complications including AL after various abdominal surgeries. CRP elevation in patients presenting acute abdomen can help classify them into different severity risk categories. Slight elevation of serum CRP level before any treatment is associated with poorer oncological outcome in some digestive cancers.

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REFERENCES

1. Clyne B, Olshaker JS. The C-reactive protein. J Emerg Med 1999;17:1019-25.
2. Holl S, Fournel I, Orry D, Facy O, Cheynel N, Rat P, *et al.* Should CT scan be performed when CRP is elevated after colorectal surgery? Results from the inflammatory markers after colorectal surgery study. J Visc Surg 2017;154:5-9.
3. Liposits G, Skuladottir H, Ryg J, Winther SB, Möller S, Hofsli E, *et al.* The Prognostic value of pre-treatment circulating biomarkers of systemic inflammation (CRP, dNLR, YKL-40, and IL-6) in vulnerable older patients with metastatic colorectal cancer receiving palliative chemotherapy-the randomized NORDIC9-study. J Clin Med 2022;11:5603.
4. Volanakis JE. Human C-reactive protein: Expression, structure, and function. Mol Immunol 2001;38:189-97.
5. Floyd-Smith G, Whitehead AS, Colten HR, Francke U. The human C-reactive protein gene (CRP) and serum amyloid *P* component gene (APCS) are located on the proximal long arm of chromosome 1. Immunogenetics 1986;24:171-6.
6. Zeller J, Bogner B, Kiefer J, Braig D, Winninger O, Fricke M, *et al.* CRP enhances the innate killing mechanisms phagocytosis and ROS formation in a conformation and complement-dependent manner. Front Immunol 2021;12:721887.
7. Kayser S, Brunner P, Althaus K, Dorst J, Sheriff A. Selective apheresis of c-reactive protein for treatment of indications with elevated CRP concentrations. J Clin Med 2020;9:2947.
8. Bilgin IA, Hatipoglu E, Aghayeva A, Arikan AE, Incir S, Mamal Torun M, *et al.* Predicting value of serum procalcitonin, C-reactive protein, drain fluid culture, drain fluid interleukin-6, and tumor necrosis factor-α levels in anastomotic leakage after rectal resection. Surg Infect (Larchmt) 2017;18:350-6.
9. Fossdal G, Mjelle AB, Wiencke K, Bjørk I, Gilja OH, Folseraas T, *et al.* Fluctuating biomarkers in primary sclerosing cholangitis: A longitudinal comparison of alkaline phosphatase, liver stiffness, and ELF. JHEP Rep 2021;3:100328.
10. Hilgenfeldt U, Kellermann W, Kienapfel G, Jochum M. Relationship between angiotensinogen, alpha 1-protease inhibitor elastase complex, antithrombin III and C-reactive protein in septic ARDS. Eur J Clin Pharmacol 1990;38:125-31.
11. Hou F, Wang L, Wang H, Gu J, Li M, Zhang J, *et al.* Elevated gene expression of S100A12 is correlated with the predominant clinical inflammatory factors in patients with bacterial pneumonia. Mol Med Rep 2015;11:4345-52.
12. Niewiadomski O, Studd C, Hair C, Wilson J, Ding NS, Heerasing N, *et al.* Prospective population-based cohort of inflammatory bowel disease in the biologics era: Disease course and predictors of severity. J Gastroenterol Hepatol 2015;30:1346-53.
13. Ołdakowska M, Ściskalska M, Kepinska M, Marek G, Milnerowicz H. Association of genetic variants in IL6 gene (rs1800795) with the concentration of inflammatory markers (IL-6, hs-CRP) and superoxide dismutase in the blood of patients with acute pancreatitis-preliminary findings. Genes (Basel) 2022;13:290.
14. Allin KH, Nordestgaard BG. Elevated C-reactive protein in the diagnosis, prognosis, and cause of cancer. Crit Rev Clin Lab Sci 2011;48:155-70.
15. Bouteloup G, Lefevre JH, Challine A, Voron T, O'Connell L, Debove C, *et al.* C-reactive protein values after surgery for inflammatory bowel disease: Is it still a good marker for intra-abdominal complication? A retrospective cohort study of 347 procedures: CRP after inflammatory bowel disease surgery. Int J Colorectal Dis 2022;37:2347-56.
16. Elborn JS, Cordon SM, Parker D, Delamere FM, Shale DJ. The host inflammatory response prior to death in patients with cystic fibrosis and chronic *Pseudomonas aeruginosa* infection. Respir Med 1993;87:603-7.
17. Kakuta K, Dohi K, Yamamoto T, Fujimoto N, Shimoyama T, Umegae S, *et al.* Coronary microvascular dysfunction restored after surgery in inflammatory bowel disease: A prospective observational study. J Am Heart Assoc 2021;10:e019125.
18. Howren MB, Lamkin DM, Suls J. Associations of depression with C-reactive protein, IL-1, and IL-6: A meta-analysis. Psychosom Med 2009;71:171-86.
19. Meynaar IA, Droog W, Batstra M, Vreede R, Herbrink P. In critically Ill patients, serum procalcitonin is more useful in differentiating between sepsis and SIRS than CRP, Il-6, or LBP. Crit Care Res Pract 2011;2011:594645.
20. Ngwa DN, Pathak A, Agrawal A. IL-6 regulates induction of C-reactive protein gene expression by activating STAT3 isoforms. Mol Immunol 2022;146:50-6.
21. Suk HJ, Ridker PM, Cook NR, Zee RY. Relation of polymorphism within the C-reactive protein gene and plasma CRP levels. Atherosclerosis 2005;178:139-45.

22. Kushner I, Agrawal A. CRP can play both pro-inflammatory and anti-inflammatory roles. Mol Immunol 2007;44:670-1.
23. Almeida AB, Faria G, Moreira H, Pinto-de-Sousa J, Correia-da-Silva P, Maia JC. Elevated serum C-reactive protein as a predictive factor for anastomotic leakage in colorectal surgery. Int J Surg 2012;10:87-91.
24. Adamina M, Steffen T, Tarantino I, Beutner U, Schmied BM, Warschkow R. Meta-analysis of the predictive value of C-reactive protein for infectious complications in abdominal surgery. Br J Surg 2015;102:590-8.
25. Lagoutte N, Facy O, Ravoire A, Chalumeau C, Jonval L, Rat P, *et al.* C-reactive protein and procalcitonin for the early detection of anastomotic leakage after elective colorectal surgery: Pilot study in 100 patients. J Visc Surg 2012;149:e345-9.
26. Paradis T, Zorigtbaatar A, Trepanier M, Fiore JF Jr., Fried GM, Feldman LS, *et al.* Meta-analysis of the diagnostic accuracy of C-reactive protein for infectious complications in laparoscopic versus open colorectal surgery. J Gastrointest Surg 2020;24:1392-401.
27. Späth C, Srinivasa S, Walsh M, Singh P, Rodgers M, Koea J. Role of post-operative serum C-reactive protein levels as a predictor of complications in upper gastrointestinal surgery. ANZ J Surg 2019;89:74-8.
28. Yeung DE, Peterknecht E, Hajibandeh S, Hajibandeh S, Torrance AW. C-reactive protein can predict anastomotic leak in colorectal surgery: A systematic review and meta-analysis. Int J Colorectal Dis 2021;36:1147-62.
29. Janet J, Derbal S, Durand Fontanier S, Bouvier S, Christou N, Fabre A, *et al.* C-reactive protein is a predictive factor for complications after incisional hernia repair using a biological mesh. Sci Rep 2021;11:4379.
30. Pochhammer J, Scholtes B, Keuler J, Müssle B, Welsch T, Schäffer M. Serum C-reactive protein level after ventral hernia repair with mesh reinforcement can predict infectious complications: A retrospective cohort study. Hernia 2020;24:41-8.
31. Aiolfi A, Asti E, Rausa E, Bonavina G, Bonitta G, Bonavina L. Use of C-reactive protein for the early prediction of anastomotic leak after esophagectomy: Systematic review and Bayesian meta-analysis. PLoS One 2018;13:e0209272.
32. Asti E, Bonitta G, Melloni M, Tornese S, Milito P, Sironi A, *et al.* Utility of C-reactive protein as predictive biomarker of anastomotic leak after minimally invasive esophagectomy. Langenbecks Arch Surg 2018;403:235-44.
33. Barbaro A, Eldredge TA, Shenfine J. Diagnosing anastomotic leak post-esophagectomy: A systematic review. Dis Esophagus 2021;34:doaa076.
34. Barrie J, Cockbain A, Tsachiridi M, Surendrakumar V, Maxwell M, Tamhankar AP. Predicting delayed complications after esophagectomy in the current era of early discharge and enhanced recovery. Am Surg 2020;86:615-20.
35. Stuart SK, Kuypers TJ, Martijnse IS, Heisterkamp J, Matthijsen RA. C-reactive protein and drain amylase: Their utility in ruling out anastomotic leakage after minimally invasive Ivor-Lewis esophagectomy. Scand J Gastroenterol 2023;58:448-52.
36. Rat P, Piessen G, Vanderbeken M, Chebaro A, Facy O, Rat P, *et al.* C-reactive protein identifies patients at low risk of anastomotic leak after esophagectomy. Langenbecks Arch Surg 2022;407:3377-86.
37. Liesenfeld LF, Sauer P, Diener MK, Hinz U, Schmidt T, Müller-Stich BP, *et al.* Prognostic value of inflammatory markers for detecting anastomotic leakage after esophageal resection. BMC Surg 2020;20:324.
38. Neary C, McAnena P, McAnena O, Kerin M, Collins C. C-reactive protein-lymphocyte ratio identifies patients at low risk for major morbidity after oesophagogastric resection for cancer. Dig Surg 2020;37:515-23.
39. Huang C, Yao H, Huang Q, Lu H, Xu M, Wu J. A novel nomogram to predict the risk of anastomotic leakage in patients after oesophagectomy. BMC Surg 2020;20:64.
40. Gordon AC, Cross AJ, Foo EW, Roberts RH. C-reactive protein is a useful negative predictor of anastomotic leak in oesophago-gastric resection. ANZ J Surg 2018;88:223-7.
41. Okubo K, Arigami T, Matsushita D, Kijima T, Shimonosono M, Uenosono Y, *et al.* Clinical impact of creatine phosphokinase and c-reactive protein as predictors of postgastrectomy complications in patients with gastric cancer. BMC Cancer 2021;21:95.
42. Tanaka H, Tamura T, Toyokawa T, Muguruma K, Kubo N, Sakurai K, *et al.* C-reactive protein elevation ratio as an early predictor of postoperative severe complications after laparoscopic gastrectomy for gastric cancer: A retrospective study. BMC Surg 2019;19:114.
43. Lee SH, Kim KH, Choi CW, Kim SJ, Kim DH, Choi CI, *et al.* Reduction rate of C-reactive protein as an early predictor of postoperative complications and a reliable discharge indicator after gastrectomy for gastric cancer. Ann Surg Treat Res 2019;97:65-73.
44. Migliore R, Gentile JK, Franca FT, Kappaz GT, Bueno-DE-Souza PM, Assef JC. Impact of bariatric surgery on the inflammatory state based on CPR value. Arq Bras Cir Dig 2018;31:e1402.
45. Askarpour M, Khani D, Sheikhi A, Ghaedi E, Alizadeh S. Effect of bariatric surgery on serum inflammatory factors of obese patients: A systematic review and meta-analysis. Obes Surg 2019;29:2631-47.
46. Thereaux J, Mingant F, Roche C, Galinat H, Couturaud F, Lacut K. Reduction of coagulability state one year after bariatric surgery. Surg Obes Relat Dis 2017;13:327-33.
47. Lee Y, McKechnie T, Doumouras AG, Handler C, Eskicioglu C, Gmora S, *et al.* Diagnostic value of C-reactive protein levels in postoperative infectious complications after bariatric surgery: A systematic review and meta-analysis. Obes Surg 2019;29:2022-9.
48. Bona D, Micheletto G, Bonitta G, Panizzo V, Cavalli M, Rausa E, *et al.* Does C-reactive protein have a predictive role in the early diagnosis of postoperative complications after bariatric surgery? Systematic review and Bayesian meta-analysis. Obes Surg 2019;29:3448-56.
49. Yang Q, Li M, Cao X, Lu Y, Tian C, Sun M, *et al.* An umbrella review of meta-analyses on diagnostic accuracy of C-reactive protein. Int J Surg 2022;104:106788.
50. Duprée A, de Heer J, Tichby M, Ghadban T, Mann O, Grupp K, *et al.* The value of CT imaging and CRP quotient for detection of postbariatric complications. Langenbecks Arch Surg 2021;406:181-7.
51. Amroun K, Deguelte S, Djerada Z, Ramont L, Perrenot C, Rached L, *et al*. High amylase concentration in drainage liquid can early predict proximal and distal intestinal anastomotic leakages: A prospective observational study. J Res Med Sci 2023;28:5. doi: 10.4103/jrms.jrms_273_21.
52. Amroun K, Scholer V, Djerada Z, Renard Y, Bouche O, Rhaiem R, *et al.* Inflammatory biomarkers to predict postoperative infectious complications after cytoreductive surgery and HIPEC for peritoneal carcinomatosis. Eur J Surg Oncol 2022;48:455-61.
53. Welsch T, Müller SA, Ulrich A, Kischlat A, Hinz U, Kienle P, *et al*. C-reactive protein as early predictor for infectious postoperative complications in rectal surgery. Int J Colorectal Dis 2007;22:1499-507.
54. Ortega-Deballon P, Radais F, Facy O, d'Athis P, Masson D, Charles PE, *et al.* C-reactive protein is an early predictor of septic complications after elective colorectal surgery. World J Surg 2010;34:808-14.
55. Pavlidis ET, Pavlidis TE. Current aspects on the management of perforated acute diverticulitis: A narrative review. Cureus 2022;14:e28446.

56. McSorley ST, Khor BY, MacKay GJ, Horgan PG, McMillan DC. Examination of a CRP first approach for the detection of postoperative complications in patients undergoing surgery for colorectal cancer: A pragmatic study. Medicine (Baltimore) 2017;96:e6133.
57. Rama NJ, Lages MC, Guarino MP, Lourenço Ó, Motta Lima PC, Parente D, *et al.* Usefulness of serum C-reactive protein and calprotectin for the early detection of colorectal anastomotic leakage: A prospective observational study. World J Gastroenterol 2022;28:2758-74.
58. McSorley ST, Roxburgh CS, Horgan PG, McMillan DC. The impact of preoperative dexamethasone on the magnitude of the postoperative systemic inflammatory response and complications following surgery for colorectal cancer. Ann Surg Oncol 2017;24:2104-12.
59. McSorley ST, Horgan PG, McMillan DC. The impact of preoperative corticosteroids on the systemic inflammatory response and postoperative complications following surgery for gastrointestinal cancer: A systematic review and meta-analysis. Crit Rev Oncol Hematol 2016;101:139-50.
60. Rompianesi G, Hann A, Komolafe O, Pereira SP, Davidson BR, Gurusamy KS. Serum amylase and lipase and urinary trypsinogen and amylase for diagnosis of acute pancreatitis. Cochrane Database Syst Rev 2017;4:CD012010.
61. Wong SS, Cheung CW. Optimization of opioid utility in cancer pain populations. Ann Palliat Med 2020;9:558-70.
62. Hirota M, Takada T, Kawarada Y, Hirata K, Mayumi T, Yoshida M, *et al.* JPN Guidelines for the management of acute pancreatitis: Severity assessment of acute pancreatitis. J Hepatobiliary Pancreat Surg 2006;13:33-41.
63. Yadav D, Agarwal N, Pitchumoni CS. A critical evaluation of laboratory tests in acute pancreatitis. Am J Gastroenterol 2002;97:1309-18.
64. Al-Bahrani AZ, Ammori BJ. Clinical laboratory assessment of acute pancreatitis. Clin Chim Acta 2005;362:26-48.
65. Walkowska J, Zielinska N, Tubbs RS, Podgórski M, Dłubek-Ruxer J, Olewnik Ł. Diagnosis and treatment of acute pancreatitis. Diagnostics (Basel) 2022;12:1974.
66. Walkowska J, Zielinska N, Karauda P, Tubbs RS, Kurtys K, Olewnik Ł. The pancreas and known factors of acute pancreatitis. J Clin Med 2022;11:5565.
67. Rau B, Pralle U, Mayer JM, Beger HG. Role of ultrasonographically guided fine-needle aspiration cytology in the diagnosis of infected pancreatic necrosis. Br J Surg 1998;85:179-84.
68. Komolafe O, Pereira SP, Davidson BR, Gurusamy KS. Serum C-reactive protein, procalcitonin, and lactate dehydrogenase for the diagnosis of pancreatic necrosis. Cochrane Database Syst Rev 2017;4:CD012645.
69. Wu S, Wu H, Xu G, Zhao Y, Xue F, Dong S, *et al.* Risk factors and clinical impacts of post-pancreatectomy acute pancreatitis after pancreaticoduodenectomy: A single-center retrospective analysis of 298 patients based on the ISGPS definition and grading system. Front Surg 2022;9:916486.
70. Lu J, Ding Y, Qu Y, Mei W, Guo Y, Fang Z, *et al.* Risk factors and outcomes of multidrug-resistant bacteria infection in infected pancreatic necrosis patients. Infect Drug Resist 2022;15:7095-106.
71. Moran RA, Jalaly NY, Kamal A, Rao S, Klapheke R, James TW, *et al.* Ileus is a predictor of local infection in patients with acute necrotizing pancreatitis. Pancreatology 2016;16:966-72.
72. Rasslan R, da Costa Ferreira Novo F, Rocha MC, Bitran A, de Souza Rocha M, de Oliveira Bernini C, *et al.* Pancreatic necrosis and gas in the retroperitoneum: Treatment with antibiotics alone. Clinics (Sao Paulo) 2017;72:87-94.
73. Greenberg JA, Hsu J, Bawazeer M, Marshall J, Friedrich JO, Nathens A, *et al.* Clinical practice guideline: Management of acute pancreatitis. Can J Surg 2016;59:128-40.
74. Ahmad R, Bhatti KM, Ahmed M, Malik KA, Rehman S, Abdulgader A, *et al.* C-Reactive protein as a predictor of complicated acute pancreatitis: Reality or a Myth? Cureus 2021;13:e19265.
75. Farkas N, Hanák L, Mikó A, Bajor J, Sarlós P, Czimmer J, *et al.* A multicenter, international cohort analysis of 1435 cases to support clinical trial design in acute pancreatitis. Front Physiol 2019;10:1092.
76. Chen HZ, Ji L, Li L, Wang G, Bai XW, Cheng CD, *et al.* Early prediction of infected pancreatic necrosis secondary to necrotizing pancreatitis. Medicine (Baltimore) 2017;96:e7487.
77. Wang B, Tang R, Wu S, Liu M, Kanwal F, Rehman MF, *et al.* Clinical value of neutrophil CD64 index, PCT, and CRP in acute pancreatitis complicated with abdominal infection. Diagnostics (Basel) 2022;12:2409.
78. Tarar MY, Khalid A, Choo XY, Khurshid S, Tumeh H, Muhammad K. Use of the C-reactive protein (CRP)/albumin ratio as a severity tool in acute pancreatitis: Systematic review. Cureus 2022;14:e29243.
79. Mintziras I, Maurer E, Kanngiesser V, Bartsch DK. C-reactive protein and drain amylase accurately predict clinically relevant pancreatic fistula after partial pancreaticoduodenectomy. Int J Surg 2020;76:53-8.
80. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, *et al.* The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. Surgery 2017;161:584-91.
81. Chen BP, Bennett S, Bertens KA, Balaa FK, Martel G. Use and acceptance of the International Study Group for Pancreatic Fistula (ISGPF) definition and criteria in the surgical literature. HPB (Oxford) 2018;20:69-75.
82. Marchegiani G, Andrianello S, Salvia R, Bassi C. Current definition of and controversial issues regarding postoperative pancreatic fistulas. Gut Liver 2019;13:149-53.
83. Miao Y, Lu Z, Yeo CJ, Vollmer CM Jr., Fernandez-Del Castillo C, Ghaneh P, *et al.* Management of the pancreatic transection plane after left (distal) pancreatectomy: Expert consensus guidelines by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 2020;168:72-84.
84. Zhao H, Liu H, Qi W, Liu W, Ye L, Cao Q, *et al.* Postoperative ratio of C-reactive protein to albumin as a predictive marker in patients with Crohn's disease undergoing bowel resection. Gastroenterol Res Pract 2021. p. 6629608.
85. Fujiwara Y, Misawa T, Shiba H, Shirai Y, Iwase R, Haruki K, *et al.* A novel postoperative inflammatory score predicts postoperative pancreatic fistula after pancreatic resection. Anticancer Res 2013;33:5005-10.
86. Malya FU, Hasbahceci M, Tasci Y, Kadioglu H, Guzel M, Karatepe O, *et al*. The Role of C-Reactive Protein in the Early Prediction of Serious Pancreatic Fistula Development after Pancreaticoduodenectomy. Gastroenterol Res Pract 20182018:9157806. doi: 10.1155/2018/9157806.
87. Yamada S, Yagi S, Sato K, Shin'e M, Sakamoto A, Utsunomiya D, *et al.* Serum C-reactive protein level on first postoperative day can predict occurrence of postoperative pancreatic fistula after laparoscopic gastrectomy. J Med Invest 2019;66:285-8.
88. Sakamoto K, Ogawa K, Tamura K, Iwata M, Matsui T, Nishi Y, *et al.* Postoperative elevation of C-reactive protein levels and high drain fluid amylase output are strong predictors of pancreatic fistulas after distal pancreatectomy. J Hepatobiliary Pancreat Sci 2021;28:874-82.
89. Guilbaud T, Garnier J, Girard E, Ewald J, Risse O, Moutardier V, *et al.* Postoperative day 1 combination of serum C-reactive protein and drain amylase values predicts risks of clinically relevant

pancreatic fistula. The "90-1000" score. Surgery 2021;170:1508-16.
90. Iwasaki T, Nara S, Kishi Y, Esaki M, Takamoto T, Shimada K. Proposal of a clinically useful criterion for early drain removal after pancreaticoduodenectomy. J Gastrointest Surg 2021;25:737-46.
91. Juez LD, Payno E, de Vicente I, Lisa E, Molina JM, Lobo Martínez E, *et al.* C-reactive protein postoperative values to predict clinically relevant postoperative pancreatic fistula after distal pancreatectomy. Rev Esp Enferm Dig 2023;115:362-7.
92. Hiyoshi M, Chijiiwa K, Fujii Y, Imamura N, Nagano M, Ohuchida J. Usefulness of drain amylase, serum C-reactive protein levels and body temperature to predict postoperative pancreatic fistula after pancreaticoduodenectomy. World J Surg 2013;37:2436-42.
93. Fukada M, Murase K, Higashi T, Yokoi R, Tanaka Y, Okumura N, *et al.* Early predictive factors for postoperative pancreatic fistula after distal pancreatectomy for pancreatic cancer. Cancer Diagn Progn 2022;2:452-61.
94. Vilhav C, Fagman JB, Holmberg E, Naredi P, Engström C. C-reactive protein identifies patients at risk of postpancreatectomy hemorrhage. Langenbecks Arch Surg 2022;407:1949-59.
95. Uchida Y, Masui T, Hashida K, Machimoto T, Nakano K, Yogo A, *et al.* Impact of vascular abnormality on contrast-enhanced CT and high C-reactive protein levels on postoperative pancreatic hemorrhage after pancreaticoduodenectomy: A multi-institutional, retrospective analysis of 590 consecutive cases. Pancreatology 2021;21:263-8.
96. Coppola A, La Vaccara V, Caggiati L, Carbone L, Spoto S, Ciccozzi M, *et al.* Utility of preoperative systemic inflammatory biomarkers in predicting postoperative complications after pancreaticoduodenectomy: Literature review and single center experience. World J Gastrointest Surg 2021;13:1216-25.
97. Giardino A, Spolverato G, Regi P, Frigerio I, Scopelliti F, Girelli R, *et al.* C-reactive protein and procalcitonin as predictors of postoperative inflammatory complications after pancreatic surgery. J Gastrointest Surg 2016;20:1482-92.
98. Chen G, Yi H, Zhang J. Diagnostic value of C-reactive protein and procalcitonin for postoperative pancreatic fistula following pancreatoduodenectomy: A systematic review and meta-analysis. Gland Surg 2021;10:3252-63.
99. Ma J, Jiang P, Ji B, Song Y, Liu Y. Post-operative procalcitonin and C-reactive protein predict pancreatic fistula after laparoscopic pancreatoduodenectomy. BMC Surg 2021;21:171.
100. Vasavada B, Patel H. Postoperative serum procalcitonin versus C-reactive protein as a marker of postoperative infectious complications in pancreatic surgery: A meta-analysis. ANZ J Surg 2021;91:E260-70.
101. Pecorelli N, Guarneri G, Palucci M, Gozzini L, Vallorani A, Crippa S, *et al.* Early biochemical predictors of clinically relevant pancreatic fistula after distal pancreatectomy: A role for serum amylase and C-reactive protein. Surg Endosc 2022;36:5431-41.
102. Kawaida H, Kono H, Amemiya H, Hosomura N, Higuchi Y, Nakayama T, *et al.* Early drain removal regardless of drain fluid amylase level might reduce risk of postoperative pancreatic fistula. Anticancer Res 2021;41:403-8.
103. Chen H, Wang W, Zou S, Wang X, Ying X, Cheng D, *et al.* Serum lipase on postoperative day one is a strong predictor of clinically relevant pancreatic fistula after pancreaticoduodenectomy: A retrospective cohort. Pancreatology 2022;22:810-6.
104. Bannone E, Marchegiani G, Perri G, Procida G, Vacca PG, Cattelani A, *et al.* Postoperative serum hyperamylasemia (POH) predicts additional morbidity after pancreatoduodenectomy: It is not all about pancreatic fistula. Surgery 2022;172:715-22.
105. Bannone E, Marchegiani G, Vollmer C, Perri G, Procida G, Corvino G, *et al.* Postoperative serum hyperamylasemia adds sequential value to the fistula risk score in predicting pancreatic fistula after pancreatoduodenectomy. Ann Surg 2023;278:e293-301.
106. de Jong KP, Hoedemakers RM, Fidler V, Bijzet J, Limburg PC, Peeters PM, *et al.* Portal and systemic serum growth factor and acute-phase response after laparotomy or partial hepatectomy in patients with colorectal liver metastases: A prognostic role for C-reactive protein and hepatocyte growth factor. Scand J Gastroenterol 2004;39:1141-8.
107. Rahman SH, Evans J, Toogood GJ, Lodge PA, Prasad KR. Prognostic utility of postoperative C-reactive protein for posthepatectomy liver failure. Arch Surg 2008;143:247-53.
108. Gyoeri GP, Pereyra D, Braunwarth E, Ammann M, Jonas P, Offensperger F, *et al.* The 3-60 criteria challenge established predictors of postoperative mortality and enable timely therapeutic intervention after liver resection. Hepatobiliary Surg Nutr 2019;8:111-24.
109. Reissfelder C, Rahbari NN, Koch M, Kofler B, Sutedja N, Elbers H, *et al.* Postoperative course and clinical significance of biochemical blood tests following hepatic resection. Br J Surg 2011;98:836-44.
110. Pattou M, Stylianos T, Nassar A, Guilbaud T, Birnbaum DJ, Tribillon E, *et al*. Est-ce que la CRP permet de diagnostiquer précocement une fistule biliaire après résection hépatique? J de Chirurgie Viscérale 2022;159:S88. [doi: 10.1016/j.jchirv.2022.07.062].
111. Fujiwara Y, Shiba H, Furukawa K, Iida T, Haruki K, Gocho T, *et al*. Glasgow prognostic score is related to blood transfusion requirements and post-operative complications in hepatic resection for hepatocellular carcinoma. Anticancer Res 2010;30:5129-36.
112. Yu J, Shi X, Ma J, Chen R, Dong S, Lu S, *et al.* C-reactive protein is an independent predictor of 30-day bacterial infection post-liver transplantation. Biomolecules 2021;11:1195.
113. Hai HH, Aw P, Teng TZJ, Shelat VG. Perioperative steroid administration reduces overall complications in patients undergoing liver resection: A meta-analysis. World J Gastrointest Surg 2021;13:1079-94.
114. Chalazonitis AN, Tzovara I, Sammouti E, Ptohis N, Sotiropoulou E, Protoppapa E, *et al.* CT in appendicitis. Diagn Interv Radiol 2008;14:19-25.
115. Krzyzak M, Mulrooney SM. Acute appendicitis review: Background, epidemiology, diagnosis, and treatment. Cureus 2020;12:e8562.
116. Perez KS, Allen SR. Complicated appendicitis and considerations for interval appendectomy. JAAPA 2018;31:35-41.
117. Di Saverio S, Podda M, De Simone B, Ceresoli M, Augustin G, Gori A, *et al.* Diagnosis and treatment of acute appendicitis: 2020 update of the WSES Jerusalem guidelines. World J Emerg Surg 2020;15:27.
118. Frountzas M, Stergios K, Kopsini D, Schizas D, Kontzoglou K, Toutouzas K. Alvarado or RIPASA score for diagnosis of acute appendicitis? A meta-analysis of randomized trials. Int J Surg 2018;56:307-14.
119. Atema JJ, van Rossem CC, Leeuwenburgh MM, Stoker J, Boermeester MA. Scoring system to distinguish uncomplicated from complicated acute appendicitis. Br J Surg 2015;102:979-90.
120. Zouari M, Louati H, Abid I, Ben Abdallah AK, Ben Dhaou M, Jallouli M, *et al.* C-reactive protein value is a strong predictor of acute appendicitis in young children. Am J Emerg Med 2018;36:1319-20.
121. Yu CW, Juan LI, Wu MH, Shen CJ, Wu JY, Lee CC. Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. Br J Surg 2013;100:322-9.
122. Blok GC, Nikkels ED, van der Lei J, Berger MY, Holtman GA. Added value of CRP to clinical features when assessing appendicitis in children. Eur J Gen Pract 2022;28:95-101.
123. Fawkner-Corbett D, Hayward G, Alkhmees M, Van Den Bruel A,

Ordóñez-Mena JM, Holtman GA. Diagnostic accuracy of blood tests of inflammation in paediatric appendicitis: A systematic review and meta-analysis. BMJ Open 2022;12:e056854.
124. Kave M, Parooie F, Salarzaei M. Pregnancy and appendicitis: A systematic review and meta-analysis on the clinical use of MRI in diagnosis of appendicitis in pregnant women. World J Emerg Surg 2019;14:37.
125. Hansson J, Khorram-Manesh A, Alwindawe A, Lundholm K. A model to select patients who may benefit from antibiotic therapy as the first line treatment of acute appendicitis at high probability. J Gastrointest Surg 2014;18:961-7.
126. Ehlers AP, Talan DA, Moran GJ, Flum DR, Davidson GH. Evidence for an antibiotics-first strategy for uncomplicated appendicitis in adults: A systematic review and gap analysis. J Am Coll Surg 2016;222:309-14.
127. Minneci PC, Mahida JB, Lodwick DL, Sulkowski JP, Nacion KM, Cooper JN, *et al.* Effectiveness of patient choice in nonoperative versus surgical management of pediatric uncomplicated acute appendicitis. JAMA Surg 2016;151:408-15.
128. CODA Collaborative, Flum DR, Davidson GH, Monsell SE, Shapiro NI, Odom SR, *et al*. A randomized trial comparing antibiotics with appendectomy for appendicitis. N Engl J Med 2020;383:1907-19.
129. Kubota A, Yokoyama N, Sato D, Hashidate H, Nojiri S, Taguchi C, *et al.* Treatment for appendicitis with appendicolith by the stone size and serum C-reactive protein level. J Surg Res 2022;280:179-85.
130. Puputti J, Suominen JS, Luoto T, Hiltunen P, Ripatti L, Nikoskelainen M, *et al*. A randomized, controlled multicenter feasibility pilot trial on imaging confirmed uncomplicated acute appendicitis: Appendectomy versus symptomatic treatment in pediatric patients (the APPSYPP) trial study protocol. Contemp Clin Trials 2022;123:106970.
131. Sippola S, Grönroos J, Sallinen V, Rautio T, Nordström P, Rantanen T, *et al*. A randomised placebo-controlled double-blind multicentre trial comparing antibiotic therapy with placebo in the treatment of uncomplicated acute appendicitis: APPAC III trial study protocol. BMJ Open 2018;8:e023623.
132. Salminen P, Paajanen H, Rautio T, Nordström P, Aarnio M, Rantanen T, *et al.* Antibiotic therapy versus appendectomy for treatment of uncomplicated acute appendicitis: The APPAC randomized clinical trial. JAMA 2015;313:2340-8.
133. Augustin G, Mikuš M, Bogdanic B, Barcot O, Herman M, Goldštajn MŠ, *et al*. A novel appendicitis TriMOdal prediction score (ATMOS) for acute appendicitis in pregnancy: A retrospective observational study. Updates Surg 2022;74:1933-41.
134. Yuksel ME, Ozkan N, Avci E. C-reactive protein/albumin ratio greater than 7.1 is a good candidate to be used as an inflammation biomarker to predict perforation in appendicitis. Eur Rev Med Pharmacol Sci 2022;26:8333-41.
135. Hou J, Feng W, Liu W, Hou J, Die X, Sun J, *et al.* The use of the ratio of C-reactive protein to albumin for the diagnosis of complicated appendicitis in children. Am J Emerg Med 2022;52:148-54.
136. Di Mitri M, Parente G, Bonfiglioli G, Thomas E, Bisanti C, Cordola C, *et al.* IL-6 serum levels can enhance the diagnostic power of standard blood tests for acute appendicitis. Children (Basel) 2022;9:1425.
137. Frongia G, Dostal F, Ziebell L, Vuille-Dit-Bille NR, Müller T, Schenk JP, *et al.* Delayed surgery for perforated appendicitis is feasible in children without compromising the outcome in selected cases. World J Surg 2022;46:1980-6.
138. Frongia G, Mehrabi A, Ziebell L, Schenk JP, Günther P. Predicting postoperative complications after pediatric perforated appendicitis. J Invest Surg 2016;29:185-94.
139. Schäfer M, Krähenbühl L, Büchler MW. Predictive factors for the type of surgery in acute cholecystitis. Am J Surg 2001;182:291-7.
140. Vural S, Aydin I, Kesicioglu T. Association of serum C-reactive protein level and treatment duration in acute cholecystitis patients treated conservatively. Cureus 2022;14:e22146.
141. Mok KW, Reddy R, Wood F, Turner P, Ward JB, Pursnani KG, *et al.* Is C-reactive protein a useful adjunct in selecting patients for emergency cholecystectomy by predicting severe/gangrenous cholecystitis? Int J Surg 2014;12:649-53.
142. Juvonen T, Kiviniemi H, Niemelä O, Kairaluoma MI. Diagnostic accuracy of ultrasonography and C reactive protein concentration in acute cholecystitis: A prospective clinical study. Eur J Surg 1992;158:365-9.
143. Nikfarjam M, Niumsawatt V, Sethu A, Fink MA, Muralidharan V, Starkey G, *et al.* Outcomes of contemporary management of gangrenous and non-gangrenous acute cholecystitis. HPB (Oxford) 2011;13:551-8.
144. Sato N, Kinoshita A, Imai N, Akasu T, Yokota T, Iwaku A, *et al.* Inflammation-based prognostic scores predict disease severity in patients with acute cholecystitis. Eur J Gastroenterol Hepatol 2018;30:484-9.
145. Kabul Gurbulak E, Gurbulak B, Akgun IE, Duzkoylu Y, Battal M, Fevzi Celayir M, *et al.* Prediction of the grade of acute cholecystitis by plasma level of C-reactive protein. Iran Red Crescent Med J 2015;17:e28091.
146. Beliaev AM, Marshall RJ, Booth M. C-reactive protein has a better discriminative power than white cell count in the diagnosis of acute cholecystitis. J Surg Res 2015;198:66-72.
147. Beliaev AM, Angelo N, Booth M, Bergin C. Evaluation of neutrophil-to-lymphocyte ratio as a potential biomarker for acute cholecystitis. J Surg Res 2017;209:93-101.
148. Mahmood F, Akingboye A, Malam Y, Thakkar M, Jambulingam P. Complicated acute cholecystitis: The role of C-reactive protein and neutrophil-lymphocyte ratio as predictive markers of severity. Cureus 2021;13:e13592.
149. Bouassida M, Zribi S, Krimi B, Laamiri G, Mroua B, Slama H, *et al.* C-reactive protein is the best biomarker to predict advanced acute cholecystitis and conversion to open surgery. A prospective cohort study of 556 cases. J Gastrointest Surg 2020;24:2766-72.
150. Asai K, Watanabe M, Kusachi S, Matsukiyo H, Saito T, Kodama H, *et al.* Changes in the therapeutic strategy for acute cholecystitis after the Tokyo guidelines were published. J Hepatobiliary Pancreat Sci 2013;20:348-55.
151. Okamoto K, Suzuki K, Takada T, Strasberg SM, Asbun HJ, Endo I, *et al.* Tokyo guidelines 2018: Flowchart for the management of acute cholecystitis. J Hepatobiliary Pancreat Sci 2018;25:55-72.
152. Miura F, Okamoto K, Takada T, Strasberg SM, Asbun HJ, Pitt HA, *et al.* Tokyo Guidelines 2018: Initial management of acute biliary infection and flowchart for acute cholangitis. J Hepatobiliary Pancreat Sci 2018;25:31-40.
153. Onoe S, Maeda A, Takayama Y, Fukami Y, Kaneoka Y. A preoperative predictive scoring system to predict the ability to achieve the critical view of safety during laparoscopic cholecystectomy for acute cholecystitis. HPB (Oxford) 2017;19:406-10.
154. Jansen S, Stodolski M, Zirngibl H, Gödde D, Ambe PC. Advanced gallbladder inflammation is a risk factor for gallbladder perforation in patients with acute cholecystitis. World J Emerg Surg 2018;13:9.
155. Chen BQ, Xie F, Chen GD, Li X, Mao X, Jia B. Value of nonenhanced CT combined with laboratory examinations in the diagnosis of acute suppurative cholecystitis treated with percutaneous cholecystostomy: A retrospective study. BMC Gastroenterol 2022;22:155.
156. Heo J, Jung MK, Cho CM, Lee SY, Ryeom HK, Chun JM, *et al.* What makes acute cholecystitis recur after removing the percutaneous cholecystostomy tube? Medicine (Baltimore) 2022;101:e28767.
157. Huang SZ, Chen HQ, Liao WX, Zhou WY, Chen JH, Li WC,

et al. Comparison of emergency cholecystectomy and delayed cholecystectomy after percutaneous transhepatic gallbladder drainage in patients with acute cholecystitis: A systematic review and meta-analysis. Updates Surg 2021;73:481-94.
158. Huang H, Zhang H, Yang D, Wang W, Zhang X. Percutaneous cholecystostomy versus emergency cholecystectomy for the treatment of acute calculous cholecystitis in high-risk surgical patients: A meta-analysis and systematic review. Updates Surg 2022;74:55-64.
159. Catena F, De Simone B, Coccolini F, Di Saverio S, Sartelli M, Ansaloni L. Bowel obstruction: A narrative review for all physicians. World J Emerg Surg 2019;14:20.
160. Pavlidis ET, Pavlidis TE. Prediction factors for ischemia of closed-loop small intestinal obstruction. World J Gastrointest Surg 2022;14:1086-8.
161. Paulson EK, Thompson WM. Review of small-bowel obstruction: The diagnosis and when to worry. Radiology 2015;275:332-42.
162. El-Awady SI, El-Nagar M, El-Dakar M, Ragab M, Elnady G. Bacterial translocation in an experimental intestinal obstruction model. C-reactive protein reliability? Acta Cir Bras 2009;24:98-106.
163. Li H, Sun D, Sun D, Xiao Z, Zhuang J, Yuan C. The diagnostic value of coagulation indicators and inflammatory markers in distinguishing between strangulated and simple intestinal obstruction. Surg Laparosc Endosc Percutan Tech 2021;31:750-5.
164. Kaçer İ, Çağlar A, Akıllı NB. The prognostic value of C-reactive protein/albumin ratio in acute mesenteric ischemia. Am Surg 2023;89:1661-7.
165. Vural V, Ozozan OV. The usefulness of inflammation-based prognostic scores for the prediction of postoperative mortality in patients who underwent intestinal resection for acute intestinal ischemia. Cureus 2019;11:e6372.
166. Cosse C, Sabbagh C, Browet F, Mauvais F, Rebibo L, Zogheib E, *et al.* Serum value of procalcitonin as a marker of intestinal damages: Type, extension, and prognosis. Surg Endosc 2015;29:3132-9.
167. Cosse C, Sabbagh C, Kamel S, Galmiche A, Regimbeau JM. Procalcitonin and intestinal ischemia: A review of the literature. World J Gastroenterol 2014;20:17773-8.
168. Groesdonk HV, Raffel M, Speer T, Bomberg H, Schmied W, Klingele M, *et al.* Elevated endothelin-1 level is a risk factor for nonocclusive mesenteric ischemia. J Thorac Cardiovasc Surg 2015;149:1436-42.e2.
169. Watkins DJ, Besner GE. The role of the intestinal microcirculation in necrotizing enterocolitis. Semin Pediatr Surg 2013;22:83-7.
170. Sahin GK, Gulen M, Acehan S, Firat BT, Isikber C, Kaya A, *et al.* Do biomarkers have predictive value in the treatment modality of the patients diagnosed with bowel obstruction? Rev Assoc Med Bras (1992) 2022;68:67-72.
171. Sabbagh C, Mauvais F, Tuech JJ, Tresallet C, Ortega-Debalon P, Mathonnet M, *et al.* Impact of a procalcitonin-based algorithm on the quality of management of patients with uncomplicated adhesion-related small bowel obstruction assessed by a textbook outcome: A multicenter cluster-randomized open-label controlled trial. BMC Gastroenterol 2022;22:90.
172. Bower KL, Lollar DI, Williams SL, Adkins FC, Luyimbazi DT, Bower CE. Small bowel obstruction. Surg Clin North Am 2018;98:945-71.
173. Nissen M, Sander V, Rogge P, Alrefai M, Tröbs RB. Meckel's diverticulum in children: A monocentric experience and mini-review of literature. Children (Basel) 2022;9:35.
174. Hansen CC, Søreide K. Systematic review of epidemiology, presentation, and management of Meckel's diverticulum in the 21st century. Medicine (Baltimore) 2018;97:e12154.
175. Peters EG, Pattamatta M, Smeets BJ, Brinkman DJ, Evers SM, de Jonge WJ, *et al.* The clinical and economical impact of postoperative ileus in patients undergoing colorectal surgery. Neurogastroenterol Motil 2020;32:e13862.
176. Collins D, Winter DC. Modern concepts in diverticular disease. J Clin Gastroenterol 2015;49:358-69.
177. Tochigi T, Kosugi C, Shuto K, Mori M, Hirano A, Koda K. Management of complicated diverticulitis of the colon. Ann Gastroenterol Surg 2018;2:22-7.
178. Azhar N, Aref H, Brorsson A, Lydrup ML, Jörgren F, Schultz JK, *et al.* Management of acute uncomplicated diverticulitis without antibiotics: Compliance and outcomes -a retrospective cohort study. BMC Emerg Med 2022;22:28.
179. Schultz JK, Yaqub S, Wallon C, Blecic L, Forsmo HM, Folkesson J, *et al.* Laparoscopic lavage versus primary resection for acute perforated diverticulitis: The SCANDIV randomized clinical trial. JAMA 2015;314:1364-75.
180. Nascimbeni R, Amato A, Cirocchi R, Serventi A, Laghi A, Bellini M, *et al.* Management of perforated diverticulitis with generalized peritonitis. A multidisciplinary review and position paper. Tech Coloproctol 2021;25:153-65.
181. Mäkelä JT, Klintrup K, Rautio T. The role of low CR*P* values in the prediction of the development of acute diverticulitis. Int J Colorectal Dis 2016;31:23-7.
182. Neri A, Fusario D, Marano L, Savelli V, Bartalini Cinughi de Pazzi A, Cassetti D, *et al.* Clinical evaluation of the Mannheim prognostic index in post-operative peritonitis: A prospective cohort study. Updates Surg 2020;72:1159-66.
183. Mäkelä JT, Klintrup K, Takala H, Rautio T. The role of C-reactive protein in prediction of the severity of acute diverticulitis in an emergency unit. Scand J Gastroenterol 2015;50:536-41.
184. Bolkenstein HE, Draaisma WA, van de Wall B, Consten E, Broeders I. Treatment of acute uncomplicated diverticulitis without antibiotics: Risk factors for treatment failure. Int J Colorectal Dis 2018;33:863-9.
185. Emile SH, Elfeki H, Sakr A, Shalaby M. Management of acute uncomplicated diverticulitis without antibiotics: A systematic review, meta-analysis, and meta-regression of predictors of treatment failure. Tech Coloproctol 2018;22:499-509.
186. Ahmadi N, Ravindran P, Kim T, Ayoubi SE, Byrne CM, Young CJ. C-reactive protein trajectory in the first 48 hours predicts the need for intervention in conservative management of acute diverticulitis. ANZ J Surg 2020;90:2036-40.
187. Kechagias A, Rautio T, Kechagias G, Mäkelä J. The role of C-reactive protein in the prediction of the clinical severity of acute diverticulitis. Am Surg 2014;80:391-5.
188. Jaung R, Kularatna M, Robertson JP, Vather R, Rowbotham D, MacCormick AD, *et al.* Uncomplicated acute diverticulitis: Identifying risk factors for severe outcomes. World J Surg 2017;41:2258-65.
189. Bolkenstein HE, van Dijk ST, Consten EC, Heggelman BG, Hoeks CM, Broeders IA, *et al.* Conservative treatment in diverticulitis patients with pericolic extraluminal air and the role of antibiotic treatment. J Gastrointest Surg 2019;23:2269-76.
190. Karentzos A, Ntourakis D, Tsilidis K, Tsoulfas G, Papavramidis T. Hinchey IA acute diverticulitis with isolated pericolic air on CT imaging; to operate or not? A systematic review. Int J Surg 2021;85:1-9.
191. Vaghiri S, Prassas D, Knoefel WT, Krieg A. Surgical management in immunosuppressed patients with sigmoid diverticulitis, still a challenge: A single-center observational study. Int J Colorectal Dis 2022;37:1909-17.
192. Mei Z, Shi L, Wang B, Yang J, Xiao Z, Du P, *et al.* Prognostic role of pretreatment blood neutrophil-to-lymphocyte ratio in advanced cancer survivors: A systematic review and meta-analysis of 66 cohort studies. Cancer Treat Rev 2017;58:1-13.

193. Shibutani M, Maeda K, Nagahara H, Fukuoka T, Nakao S, Matsutani S, *et al.* The peripheral monocyte count is associated with the density of tumor-associated macrophages in the tumor microenvironment of colorectal cancer: A retrospective study. BMC Cancer 2017;17:404.
194. Hai Y, Chen N, Wu W, Wang Z, Lin F, Guo C, *et al.* High postoperative monocyte indicates inferior clinicopathological characteristics and worse prognosis in lung adenocarcinoma or squamous cell carcinoma after lobectomy. BMC Cancer 2018;18:1011.
195. Qi Q, Geng Y, Sun M, Wang P, Chen Z. Clinical implications of systemic inflammatory response markers as independent prognostic factors for advanced pancreatic cancer. Pancreatology 2015;15:145-50.
196. Hu B, Yang XR, Xu Y, Sun YF, Sun C, Guo W, *et al.* Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. Clin Cancer Res 2014;20:6212-22.
197. Allin KH, Bojesen SE, Nordestgaard BG. Baseline C-reactive protein is associated with incident cancer and survival in patients with cancer. J Clin Oncol 2009;27:2217-24.
198. Mahmoud FA, Rivera NI. The role of C-reactive protein as a prognostic indicator in advanced cancer. Curr Oncol Rep 2002;4:250-5.
199. Zhu M, Ma Z, Zhang X, Hang D, Yin R, Feng J, *et al.* C-reactive protein and cancer risk: A pan-cancer study of prospective cohort and Mendelian randomization analysis. BMC Med 2022;20:301.
200. Hart PC, Rajab IM, Alebraheem M, Potempa LA. C-reactive protein and cancer-diagnostic and therapeutic insights. Front Immunol 2020;11:595835.
201. Shrotriya S, Walsh D, Bennani-Baiti N, Thomas S, Lorton C. C-reactive protein is an important biomarker for prognosis tumor recurrence and treatment response in adult solid tumors: A systematic review. PLoS One 2015;10:e0143080.
202. Badakhshi H, Kaul D, Zhao KL. Association between the inflammatory biomarker, C-reactive protein, and the response to radiochemotherapy in patients with esophageal cancer. Mol Clin Oncol 2016;4:643-7.
203. Balkwill F, Mantovani A. Inflammation and cancer: Back to Virchow? Lancet 2001;357:539-45.
204. Coussens LM, Werb Z. Inflammation and cancer. Nature 2002;420:860-7.
205. Ernstoff MS, Crocenzi TS, Seigne JD, Crosby NA, Cole BF, Fisher JL, *et al.* Developing a rational tumor vaccine therapy for renal cell carcinoma: Immune yin and yang. Clin Cancer Res 2007;13:733s-40s.
206. Jones JM, McGonigle NC, McAnespie M, Cran GW, Graham AN. Plasma fibrinogen and serum C-reactive protein are associated with non-small cell lung cancer. Lung Cancer 2006;53:97-101.
207. Barber MD, Powell JJ, Lynch SF, Gough NJ, Fearon KC, Ross JA. Two polymorphisms of the tumour necrosis factor gene do not influence survival in pancreatic cancer. Clin Exp Immunol 1999;117:425-9.
208. Marsik C, Kazemi-Shirazi L, Schickbauer T, Winkler S, Joukhadar C, Wagner OF, *et al.* C-reactive protein and all-cause mortality in a large hospital-based cohort. Clin Chem 2008;54:343-9.
209. Sugimoto A, Toyokawa T, Miki Y, Yoshii M, Tamura T, Sakurai K, *et al.* Preoperative C-reactive protein to albumin ratio predicts anastomotic leakage after esophagectomy for thoracic esophageal cancer: A single-center retrospective cohort study. BMC Surg 2021;21:348.
210. Toiyama Y, Shimura T, Yasuda H, Fujikawa H, Okita Y, Kobayashi M, *et al.* Clinical burden of C-reactive protein/albumin ratio before curative surgery for patients with gastric cancer. Anticancer Res 2016;36:6491-8.
211. Alsaif SH, Rogers AC, Pua P, Casey PT, Aherne GG, Brannigan AE, *et al.* Preoperative C-reactive protein and other inflammatory markers as predictors of postoperative complications in patients with colorectal neoplasia. World J Surg Oncol 2021;19:74.
212. Wang W, Gu J, Liu Y, Liu X, Jiang L, Wu C, *et al.* Pre-treatment CRP-albumin-lymphocyte index (CALLY Index) as a prognostic biomarker of survival in patients with epithelial Ovarian cancer. Cancer Manag Res 2022;14:2803-12.
213. Marimuthu K, Varadhan KK, Ljungqvist O, Lobo DN. A meta-analysis of the effect of combinations of immune modulating nutrients on outcome in patients undergoing major open gastrointestinal surgery. Ann Surg 2012;255:1060-8.
214. Okamoto Y, Okano K, Izuishi K, Usuki H, Wakabayashi H, Suzuki Y. Attenuation of the systemic inflammatory response and infectious complications after gastrectomy with preoperative oral arginine and omega-3 fatty acids supplemented immunonutrition. World J Surg 2009;33:1815-21.
215. Giger U, Büchler M, Farhadi J, Berger D, Hüsler J, Schneider H, *et al.* Preoperative immunonutrition suppresses perioperative inflammatory response in patients with major abdominal surgery-a randomized controlled pilot study. Ann Surg Oncol 2007;14:2798-806.
216. STARSurg Collaborative. Impact of postoperative non-steroidal anti-inflammatory drugs on adverse events after gastrointestinal surgery. Br J Surg 2014;101:1413-23.
217. Bert M, Devilliers H, Orry D, Rat P, Facy O, Ortega-Deballon P. Preoperative inflammation is an independent factor of worse prognosis after colorectal cancer surgery. J Visc Surg 2021;158:305-11.
218. Gebauer N, Ziehm M, Gebauer J, Riecke A, Meyhöfer S, Kulemann B, *et al.* The Glasgow prognostic score predicts survival outcomes in neuroendocrine neoplasms of the Gastro-Entero-Pancreatic (GEP-NEN) system. Cancers (Basel) 2022;14:5465.
219. Eren T. Prognostic significance of the preoperative lymphocyte to C-reactive protein ratio in patients with stage III colorectal cancer. ANZ J Surg 2022;92:2585-94.
220. Minichsdorfer C, Gleiss A, Aretin MB, Schmidinger M, Fuereder T. Serum parameters as prognostic biomarkers in a real world cancer patient population treated with anti PD-1/PD-L1 therapy. Ann Med 2022;54:1339-49.
221. Lorton CM, Higgins L, O'Donoghue N, Donohoe C, O'Connell J, Mockler D, *et al.* C-reactive protein and C-reactive protein-based scores to predict survival in esophageal and junctional adenocarcinoma: Systematic review and meta-analysis. Ann Surg Oncol 2022;29:1853-65.
222. Zhou J, Wei W, Hou H, Ning S, Li J, Huang B, *et al.* Prognostic value of C-reactive protein, Glasgow prognostic score, and C-reactive protein-to-albumin ratio in colorectal cancer. Front Cell Dev Biol 2021;9:637650.
223. Yamada S, Fujii T, Yabusaki N, Murotani K, Iwata N, Kanda M, *et al.* Clinical implication of inflammation-based prognostic score in pancreatic cancer: Glasgow prognostic score is the most reliable parameter. Medicine (Baltimore) 2016;95:e3582.
224. Nurmi AM, Mustonen H, Haglund C, Seppänen H. Changes in CRP and CA19-9 during preoperative oncological therapy predict postoperative survival in pancreatic ductal adenocarcinoma. Oncology 2021;99:686-98.
225. Yu Q, Li KZ, Fu YJ, Tang Y, Liang XQ, Liang ZQ, *et al.* Clinical significance and prognostic value of C-reactive protein/albumin ratio in gastric cancer. Ann Surg Treat Res 2021;100:338-46.
226. Otowa Y, Nakamura T, Yamazaki Y, Takiguchi G, Nakagawa A,

Yamamoto M, *et al*. Meaning of C-reactive protein around esophagectomy for cStage III esophageal cancer. Surg Today 2019;49:90-5.
227. Iwasaki Y, Ishizuka M, Kato M, Kita J, Shimoda M, Kubota K. Usefulness of an inflammation-based prognostic score (mGPS) for predicting survival in patients with unresectable malignant biliary obstruction. World J Surg 2013;37:2222-8.
228. Maurer E, Heinzel-Gutenbrunner M, Rinke A, Rütz J, Holzer K, Figiel J, *et al*. Relevant prognostic factors in patients with stage IV small intestine neuroendocrine neoplasms. J Neuroendocrinol 2022;34:e13076.
229. Matsunaga T, Miyata H, Sugimura K, Motoori M, Asukai K, Yanagimoto Y, *et al*. Prognostic significance of C-reactive protein-to-prealbumin ratio in patients with esophageal cancer. Yonago Acta Med 2020;63:8-19.
230. Lu J, Xu BB, Xue Z, Xie JW, Zheng CH, Huang CM, *et al*. Perioperative CRP: A novel inflammation-based classification in gastric cancer for recurrence and chemotherapy benefit. Cancer Med 2021;10:34-44.
231. Björkman K, Kaprio T, Beilmann-Lehtonen I, Stenman UH, Böckelman C, Haglund C. TATI, TAT-2, and CRP as prognostic factors in colorectal cancer. Oncology 2022;100:22-30.
232. Hidayat F, Labeda I, Sampetoding S, Pattelongi IJ, Lusikooy RE, Warsinggih, *et al*. Correlation of interleukin-6 and C-reactive protein levels in plasma with the stage and differentiation of colorectal cancer: A cross-sectional study in East Indonesia. Ann Med Surg (Lond) 2021;62:334-40.
233. Matsubara D, Arita T, Nakanishi M, Kuriu Y, Murayama Y, Kudou M, *et al*. The impact of postoperative inflammation on recurrence in patients with colorectal cancer. Int J Clin Oncol 2020;25:602-13.
234. Hermunen K, Soveri LM, Boisen MK, Mustonen HK, Dehlendorff C, Haglund CH, *et al*. Postoperative serum CA19-9, YKL-40, CRP and IL-6 in combination with CEA as prognostic markers for recurrence and survival in colorectal cancer. Acta Oncol 2020;59:1416-23.
235. Egenvall M, Mörner M, Martling A, Gunnarsson U. Prediction of outcome after curative surgery for colorectal cancer: Preoperative haemoglobin, C-reactive protein and albumin. Colorectal Dis 2018;20:26-34.
236. Peng J, Zhang R, Zhao Y, Wu X, Chen G, Wan D, *et al*. Prognostic value of preoperative prognostic nutritional index and its associations with systemic inflammatory response markers in patients with stage III colon cancer. Chin J Cancer 2017;36:96.
237. Utsumi M, Inagaki M, Kitada K, Tokunaga N, Kondo M, Yunoki K, *et al*. Lymphocyte-to-C-reactive protein ratio predicts prognosis in patients with colorectal liver metastases post-hepatic resection: A retrospective study. Anticancer Res 2022;42:4963-71.
238. Loosen SH, Roderburg C, Alizai PH, Roeth AA, Schmitz SM, Vucur M, *et al*. Comparative analysis of circulating biomarkers for patients undergoing resection of colorectal liver metastases. Diagnostics (Basel) 2021;11:1999.
239. Frühling P, Urdzik J, Strömberg C, Isaksson B. Composite score: Prognostic tool to predict survival in patients undergoing surgery for colorectal liver metastases. BJS Open 2021;5:zrab104.
240. Deng Y, Zhao Y, Qin J, Huang X, Wu R, Zhou C, *et al*. Prognostic value of the C-reactive protein/albumin ratio and systemic immune-inflammation index for patients with colorectal liver metastasis undergoing curative resection. Pathol Oncol Res 2021;27:633480.
241. van Dijk DP, Krill M, Farshidfar F, Li T, Rensen SS, Olde Damink SW, *et al*. Host phenotype is associated with reduced survival independent of tumour biology in patients with colorectal liver metastases. J Cachexia Sarcopenia Muscle 2019;10:123-30.
242. Turpin A, Hebbar M. ASO author reflections: Fong's score in the era of modern strategies for metastatic colorectal cancer. Ann Surg Oncol 2020;27:886.
243. Matsumoto T, Kitano Y, Imai K, Kinoshita S, Sato H, Shiraishi Y, *et al*. Clinical significance of preoperative inflammation-based score for the prognosis of patients with hepatocellular carcinoma who underwent hepatectomy. Surg Today 2022;52:1008-15.
244. Asakura R, Yanagimoto H, Ajiki T, Tsugawa D, Mizumoto T, So S, *et al*. Prognostic impact of inflammation-based scores for extrahepatic cholangiocarcinoma. Dig Surg 2022;39:65-74.
245. Zhang YF, Lu LH, Zhong C, Chen MS, Guo RP, Wang L. Prognostic value of the preoperative lymphocyte-C-reactive protein ratio in hepatocellular carcinoma patients treated with curative intent: A large-scale multicentre study. J Inflamm Res 2021;14:2483-95.
246. Iseda N, Itoh S, Yoshizumi T, Tomiyama T, Morinaga A, Shimagaki T, *et al*. Lymphocyte-to-C-reactive protein ratio as a prognostic factor for hepatocellular carcinoma. Int J Clin Oncol 2021;26:1890-900.
247. Yugawa K, Itoh S, Yoshizumi T, Morinaga A, Iseda N, Toshima T, *et al*. Lymphocyte-C-reactive protein ratio as a prognostic marker associated with the tumor immune microenvironment in intrahepatic cholangiocarcinoma. Int J Clin Oncol 2021;26:1901-10.
248. Lu LH, Zhong C, Wei W, Li SH, Mei J, Zou JW, *et al*. Lymphocyte-C-reactive protein ratio as a novel prognostic index in intrahepatic cholangiocarcinoma: A multicentre cohort study. Liver Int 2021;41:378-87.
249. Wang Y, Li Z, Huang Z, Yu X, Zheng L, Xu J. C-reactive protein is an indicator of the immunosuppressive microenvironment fostered by myeloid cells in hepatocellular carcinoma. Front Oncol 2021;11:774823.