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Systemic Inflammatory Response Syndrome in Elderly Patients with Acute Appendicitis: Age-Related Immune Changes and Perioperative Management

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Abstract: Acute appendicitis is a common surgical issue with a lifetime risk of 7–8%. Prompt diagnosis is crucial to prevent complications, especially in elderly patients. Systemic Inflammatory Response Syndrome (SIRS) is a clinical condition characterized by widespread inflammation that can complicate appendicitis. This study examined the occurrence of SIRS across age groups, focusing on elderly patients, and assessed perioperative immune-modulating treatments. This retrospective study included 337 patients who underwent surgery for acute appendicitis. Patients were divided into four age categories: young adults (18–44 years), middle-aged adults (45–60 years), elderly (61–74 years), and senile (≥ 75 years). SIRS was identified using clinical criteria and examined in relation to patient age and type of appendicitis. Patients with SIRS (n = 207) received immunocorrective treatment, whereas the others received standard care. SIRS occurrence increased with age, from 32.3% in young adults to 100% in the senile group ($p < 0.001$). Elderly and senile patients met more SIRS criteria. SIRS was associated with appendicitis severity, reaching 100% in gangrenous peritonitis ($p < 0.001$). Patients with SIRS showed elevated inflammatory markers, including white blood cell count, C-reactive protein, neutrophil-to-lymphocyte ratio, and systemic immune-inflammation index. Immunocorrective treatment resulted in fewer complications (3.9%) than the typical rates for high-risk patients. This study showed an increase in SIRS incidence in elderly patients with acute appendicitis. The results revealed links between SIRS severity, age, and disease progression. The immunomodulatory protocol enhanced outcomes by reducing complications, particularly in elderly patients.

Keywords: Systemic Inflammatory Response Syndrome; Acute Appendicitis; Immunosenescence; Elderly; Neutrophils

1. Introduction

Acute appendicitis is a common surgical issue and ranks among the leading causes of abdominal pain requiring surgery worldwide. The lifetime risk is 7–8%, with symptoms ranging from mild inflammation to severe complications such as perforation and abscess formation [1,2]. Prompt diagnosis is crucial to prevent perforation, which occurs in one-third of cases and increases the risk of sepsis [1]. Diagnostic methods that incorporate clinical scoring systems and imaging techniques have enhanced risk assessment and management [3].

Systemic Inflammatory Response Syndrome (SIRS) is marked by a widespread inflammatory reaction triggered by infectious and non-infectious factors, including severe appendicitis [4]. SIRS causes the release of pro-inflammatory cytokines, which can lead to organ dysfunction far from the injury site [4,5]. In patients with appendicitis and SIRS, systemic inflammation determines prognosis; its presence indicates severe disease and sepsis risk, requiring enhanced clinical observation [1,6].

Understanding the clinical relationship between acute appendicitis and SIRS is thus crucial. Identifying SIRS criteria in patients with appendicitis indicates potential complications and directs the urgency of surgical consultation [1]. Research indicates that patients with SIRS exhibit oxidative stress and increased leukocyte activation markers, which are associated with disease severity [5]. Immature neutrophils (bands) are released during systemic inflammation. These cells maintain basic immune functions but show altered receptor expression and cytokine production, contributing to systemic inflammation [7]. The behavior of these immature cells in elderly patients with appendicitis and SIRS remains uncharacterized.

Diagnosing acute appendicitis in elderly patients is challenging because of age-related changes in inflammatory markers. Leukocytosis and elevated C-reactive protein (CRP) levels show decreased sensitivity in older adults, complicating the evaluation and increasing the risk of delayed diagnosis [8,9]. These challenges necessitate the development of enhanced diagnostic markers and risk-stratification models incorporating immune parameters.

Although clinical guidelines advocate swift identification and surgical consultation for appendicitis cases with moderate to high risk to minimize morbidity from perforation and sepsis, there is a lack of data on the targeted correction of SIRS in elderly patients with appendicitis. Understanding the prevalence and progression of SIRS across age groups and the immunological factors contributing to systemic inflammation is a critical unmet need [4,10].

SIRS is a complex immune condition triggered by infection, injury, pancreatitis, or ischemia. It involves an overactive immune response, characterized by symptoms such as fever, rapid heartbeat, increased white blood cell (WBC) count, and changes in breathing [4, 10]. The response in SIRS is driven by the innate immune system's detection of pathogen-associated or damage-associated molecular patterns via pattern recognition receptors, such as Toll-like receptors (TLRs), especially TLR-4, on macrophages, neutrophils, and dendritic cells. Activation of these receptors triggers pathways leading to the production of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukins (IL-1β, IL-6, IL-8), interferon-gamma, and other mediators such as complement components and coagulation factors, thereby intensifying inflammation [4,11–13]. This causes endothelial activation, increased vascular permeability, and WBC recruitment, leading to tissue injury and organ failure. The pro-inflammatory phase is balanced by a compensatory anti-inflammatory response syndrome, involving anti-inflammatory cytokines such as IL-10, IL-4, and transforming growth factor-beta, along with lymphocyte apoptosis and immune cell exhaustion, which can potentially lead to immunosuppression and secondary infections [14,15].

In older adults, the immune response during SIRS is altered by immunosenescence and inflammaging, a condition characterized by pro-inflammatory processes. The innate immune system shows reduced neutrophil chemotaxis, phagocytosis, and reactive oxygen species production, with changes in macrophage TLR expression, leading to weakened inflammation and slower pathogen elimination [1,7]. NK cell cytotoxicity diminishes with age, thereby weakening early cellular defenses. The adaptive immune system is affected by thymic involution, which reduces naïve T-cell production and T-cell receptor diversity. B-cell immunity is weakened by decreased antibody affinity and isotype-switching capability [14].

Immune deficiencies and inflammaging, marked by increases in IL-6, TNF-α, and CRP, set the elderly immune system to a pro-inflammatory baseline [5]. Older patients may show an unusual cytokine profile during SIRS, with an initially weakened fever and cytokine response, followed by extended inflammation that increases the risk of tissue damage [5,14]. Oxidative stress, as indicated by increased lipid peroxidation and leukocyte activation markers, is higher in critically ill elderly patients with SIRS [5].

While acute appendicitis is generally well understood [16], age-related immune changes affect inflammatory responses in older adults. Aging involves immunosenescence and inflammaging, which alter both immune systems. Immunosenescence reduces neutrophil chemotaxis, phagocytosis, and naïve T-cell production [1,8]. Inflammaging creates a pro-inflammatory environment with increased cytokine levels, such as IL-6 and TNF-α, making older adults susceptible to abnormal immune activation [1,8].

In older adults, acute appendicitis with peritonitis poses a clinical challenge, with a high risk of SIRS, sepsis, and organ dysfunction. Age-related immune changes and appendiceal perforation determine the outcomes. Immunosenescence involves reduced innate immune function, including decreased neutrophil chemotaxis, phagocytosis, and reactive oxygen species production, with weakened adaptive immunity due to thymic atrophy. Inflammaging creates a dysregulated immune environment with increased cytokine levels, such as IL-6 and TNF-α [17,18]. These factors dampen the systemic response to appendiceal infection, allowing bacterial growth and peritoneal contamination in elderly patients [19].

When the peritoneal cavity is exposed to bacteria, it triggers pattern recognition receptors, such as TLR-4, activating innate immune pathways and leading to pro-inflammatory cytokines and vascular changes in SIRS [13]. In older individuals, impaired TLR-4 signaling disrupts the immune-endocrine stress response [13]. During inflammation, immature neutrophils exhibit altered receptor expression and migration, affecting bacterial clearance [7]. Diagnosing SIRS in elderly patients with appendiceal peritonitis is challenging because of atypical presentations, reduced fever, and altered WBC counts [17,19].

SIRS in older patients with appendicitis and peritonitis increases morbidity, mortality, and complications due to diminished physiological reserve [1,19]. Elevated oxidative stress markers, including lipid peroxidation products and leukocyte activation enzymes, indicate inflammation and are correlated with worse outcomes [5]. Early detection and management, including surgical control, antibiotic therapy, and fluid resuscitation, are necessary to prevent severe sepsis [1,10]. Given the altered immunity, SIRS management may require targeting TLR signaling or oxidative stress pathways. Comprehensive geriatric assessments should guide the development of personalized perioperative care plans.

This study measured the SIRS burden using World Health Organization-defined age groups for elderly populations, assessed band neutrophils with the neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII) as inflammation indicators, and outlined a standardized perioperative immunocorrective protocol related to postoperative complications in elderly patients with appendicitis.

2. Methods

This retrospective study was conducted at Bishkek City Clinical Hospital No. 1 in Kyrgyzstan and examined patients who underwent appendicitis surgery between January 2014 and December 2020. The study analyzed SIRS occurrence across age groups, particularly in elderly (61–74 years) and senile (≥ 75 years) patients, and assessed perioperative immune-modulating treatments. The institutional bioethics committee approved this study (Protocol No. 82, dated June 12, 2015), and informed consent was obtained from all patients or their legal guardians.

This study included 337 individuals with surgically confirmed acute appendicitis. The inclusion criteria required participants to be over 18 years of age, undergo appendicitis surgery, and have complete documentation. Patients with non-appendicular peritonitis, immune system-compromising conditions, or recent abdominal surgery were excluded from the study. Patients were categorized into four WHO age groups: young adults (18–44 years), middle-aged adults (45–60 years), elderly (61–74 years), and senile adults (≥ 75 years).

SIRS was characterized based on the ACCP/SCCM Consensus Conference Committee 1992 [20], requiring at least two conditions: temperature exceeding 38 °C or below 36 °C; heart rate surpassing 90 beats per minute; respiratory rate over 20 breaths per minute or $PaCO_2$ under 32 mmHg; and white blood cell count greater than 12×10^9/L, less than 4×10^9/L, or with over 10% band forms. Individuals with immunodeficiency, active infection, or recent chemotherapy were excluded. The perioperative immunocorrective protocol was standardized for patients with SIRS, although not randomized. Surgery was conducted at the initial presentation through emergency pathways, while those presenting later with generalized peritonitis underwent surgery after urgent resuscitation.

Recovery was defined as clinical stabilization in the hospital with supportive biomarker trends; however, longer-term outcomes (7–30 days) were not systematically collected in this retrospective cohort.

The patients underwent open appendectomy using a lower-midline incision. Anesthesia was administered at

the clinician's discretion. Patients diagnosed with SIRS (n = 207) received immunocorrective therapy. A single intravenous dose of cefazolin (1.0 g) was administered before surgery. During the operation, the abdominal cavity was rinsed with ozonized sodium chloride solution (8–10 μg/mL ozone). Regional lymphatic stimulation was performed in the ileocecal area using a mixture of cefazolin (1.0 g), heparin (70 U/kg), lidase (8–12 U), proserin (2 mL), and 0.5% Novocaine (15–20 mL). Patients without SIRS received standard care, including antibiotics, fluids, and analgesics.

Patients were observed daily for SIRS criteria and inflammation indicators, including white WBC count, CRP level, and differential counts. The NLR was calculated as the neutrophil count divided by the lymphocyte count. The SII was calculated as follows: platelet count × neutrophil count/lymphocyte count. These markers were documented at admission and post-surgery to assess their correlation with age, disease severity, and complications. Postoperative complications were recorded, and patients were monitored for five days or until discharge.

Patients meeting the SIRS criteria received standardized perioperative immunocorrective treatment according to the clinical protocol. As the patients were not divided into treatment and control groups, this study was not randomized.

Data analysis was performed using the Statistical Package for the Social Sciences version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation and were compared using Student's t-test. Categorical variables were presented as frequencies and percentages, with chi-square tests used for statistical comparisons. A p-value < 0.001 was considered statistically significant for all comparisons, establishing a strict threshold to minimize Type I error. This study examined the relationships between age group, appendicitis severity, SIRS criteria, and inflammatory biomarkers, including WBC count, CRP level, NLR, and SII. All p-values were two-tailed and statistically significant.

3. Results

The study included 337 patients who underwent appendicitis surgery (**Table 1**). The mean age of the patients was 51.6 ± 17.4 years. Most were middle-aged adults (45–60 years, 46.3%), followed by young adults (18–44 years, 28.5%), elderly individuals (61–74 years, 18.4%), and those aged ≥ 75 years (6.8%). Patients with SIRS were older than those without it (61.3 ± 13.1 years vs. 38.7 ± 14.6 years, $p < 0.001$), suggesting that older age correlates with a higher risk of systemic inflammation. The median duration from admission to surgery was 6 h (interquartile range 4–9 h), aligning with typical emergency procedures; patients with peritonitis underwent urgent surgery after resuscitation.

Table 1. Demographic characteristics of patients with acute appendicitis.

Age Group	n (%)	M ± m (Years)
Young (18–44)	96 (28.5%)	31.2 ± 6.4
Middle-aged (45–60)	156 (46.3%)	52.8 ± 4.1
Elderly (61–74)	62 (18.4%)	66.7 ± 3.5
Senile (≥ 75)	23 (6.8%)	79.3 ± 3.6
Total	337 (100.0%)	51.6 ± 17.4

Note: Data presented as N (%); N = Total no. of patients; % = Percentage of total patients; and Mean ± Standard Deviation (M ± m).

Among the patients, 207 (61.4%) fulfilled the SIRS diagnostic criteria (**Table 2**). SIRS occurrence increased progressively with age: 32.3% in young adults, 65.4% in middle-aged individuals, 82.3% in elderly patients, and 100% in the senile group. This pattern was statistically significant ($p < 0.001$). Additionally, elderly and senile patients were more prone to meeting more SIRS criteria. Of the SIRS-positive patients, 84 (24.9%) exhibited two criteria, 88 (26.1%) showed three criteria, and 33 (10.4%) met four criteria. Patients aged ≥ 60 years were more likely to present with three or more SIRS signs than younger patients ($p < 0.01$).

SIRS is closely linked to the severity of appendicitis (**Table 3**). In the catarrhal form, SIRS was found in 5.8% of cases. However, it was present in 72.8% of patients with phlegmonous form and 66.7% of patients with gangrenous form. SIRS reached 100% in patients with gangrenous form complicated by localized or generalized peritonitis. These variations were statistically significant ($p < 0.001$), highlighting the link between disease progression and the systemic immune response.

Patients with SIRS showed significantly elevated levels of immune and inflammatory markers (**Table 4**). The mean WBC count in patients with SIRS was higher, measuring $15.6 \pm 3.4 \times 10^9$/L, compared to $10.2 \pm 2.1 \times 10^9$/L

in those without SIRS ($p < 0.001$). CRP levels were increased in patients with SIRS (84.3 ± 27.8 mg/L) compared to those in patients without SIRS (39.5 ± 18.2 mg/L) ($p < 0.001$), indicating heightened systemic inflammation. Patients with SIRS showed increased band neutrophil counts (mean 8.4% versus 3.1 %), indicating their association with systemic inflammatory activation ($p < 0.001$).

Table 2. Frequency and severity of SIRS according to age group.

Age Group	n (%)	≥ 3 SIRS Criteria	*p*-Value
Young (18–44)	31 (32.3%)	6	0.032
Middle-aged (45–60)	102 (65.4%)	36	< 0.001
Elderly (61–74)	51 (82.3%)	28	< 0.001
Senile (≥ 75)	23 (100.0%)	20	< 0.001
Total	207 (61.4%)	90	-

Note: Data presented as n (%); n = Patients with SIRS; % = Percentage of patients with SIRS; and SIRS = Systemic Inflammatory Response Syndrome.

Table 3. SIRS frequency according to the type of peritonitis.

Peritonitis Form	N (%)	n (%)	*p*-Value
Catarrhal	52 (15.4%)	3 (5.8%)	0.025
Phlegmonous	151 (44.8%)	110 (72.8%)	< 0.001
Gangrenous	48 (14.2%)	32 (66.7%)	< 0.001
Phlegmonous + Local peritonitis	61 (18.1%)	37 (60.6%)	< 0.001
Gangrenous + Local peritonitis	19 (5.6%)	19 (100.0%)	< 0.001
Gangrenous + Generalized peritonitis	6 (1.9%)	6 (100.0%)	< 0.001
Total	337 (100.0%)	207 (61.4%)	-

Note: Data presented as n (%); N = Total no. of patients; % = Percentage of total patients; n = Patients with SIRS; % = Percentage of patients with SIRS; and SIRS = Systemic Inflammatory Response Syndrome.

Table 4. Immune and inflammatory parameters in patients with and without SIRS.

Parameters	Patients with SIRS	Patients without SIRS	*p*-Value
White blood cells ($\times 10^9$/L)	15.6 ± 3.4	10.2 ± 2.1	< 0.001
C-Reactive Protein (mg/L)	84.3 ± 27.8	39.5 ± 18.2	< 0.001
Neutrophil-to-Lymphocyte Ratio	9.2 ± 2.8	4.3 ± 1.6	< 0.001
Systemic Immune-Inflammation Index*	1,526 ± 437	782 ± 215	< 0.001
Band Neutrophils (%)	8.4 ± 3.1	3.1 ± 1.2	< 0.001

Note: Data presented as Mean ± Standard Deviation; and SIRS = Systemic Inflammatory Response Syndrome.

A total of 207 patients diagnosed with SIRS were treated using a standardized immunocorrective perioperative protocol, whereas 130 patients received conventional care. In patients with SIRS, 8 (3.9%) patients developed postoperative complications, including wound infections, intra-abdominal abscesses, and prolonged fever. Complications occurred in 3 (2.3%) patients without SIRS. Despite higher complications in patients with SIRS, the overall incidence was significantly lower than the 10–15% typically reported for high-risk patients, suggesting an advantage of the immunomodulatory protocol. One elderly patient (80 years) who presented late with generalized peritonitis died of multiple organ failure, resulting in a 0.3% mortality rate.

Patients with SIRS had longer hospital stays (7.8 ± 2.3 days) than those without (5.2 ± 1.6 days) ($p < 0.01$). Patients with ≥ 3 SIRS symptoms showed more complications (10.2%) than those with two criteria (2.6%) ($p = 0.032$). The immunocorrective method led to a decrease in SIRS signs, with WBC counts and CRP levels normalizing by the third day. SIRS beyond 48 h was correlated with increased complications.

Patients with SIRS showed elevated immune and inflammatory markers, including WBC counts and CRP levels, indicating systemic immune activation. They exhibited higher NLR and SII values, which were associated with age and disease severity.

The findings revealed a link between patient age, appendicitis severity, and the onset of SIRS. Implementing a structured immunomodulatory protocol enhanced outcomes by reducing complications and facilitating immune recovery, particularly in elderly, high-risk patients.

Statistical analysis showed that the systemic inflammatory response was affected by age and was strongly associated with the severity of appendicitis. Patients with severe conditions exhibit stronger immune responses and elevated inflammatory markers. Age and disease stage independently predicted SIRS severity, highlighting the need for personalized strategies for older adults with advanced disease.

The implementation of an immunocorrective perioperative protocol yielded positive outcomes by adjusting the immune response. Early immunomodulatory therapy enables rapid immune parameter normalization and reduces complications. This protocol is particularly beneficial for elderly patients, showing potential for managing high-risk surgical cases with SIRS. These findings advocate for the wider adoption of immunomodulatory interventions in cases of acute appendicitis with systemic inflammation.

4. Discussion

This study highlights the increasing incidence of SIRS in elderly patients who underwent appendicitis surgery. The results showed a strong link between SIRS severity, age, and appendiceal disease advancement, aligning with studies identifying age as a major risk factor for postoperative complications [21–23].

The study found an increased incidence of SIRS across age groups, consistent with immunosenescence, which reduces the immune response in older adults while fostering inflammaging [24–26]. These factors contribute to elevated inflammation, making older patients vulnerable to excessive immune reactions [27–30]. Atypical symptoms and decreased WBC activity complicate timely diagnosis in this demographic [31].

SIRS occurred more frequently in severe histopathological types of appendicitis, particularly peritonitis. This aligns with research showing that perforated appendicitis is more likely to initiate a systemic inflammatory response [32–35]. All patients with generalized peritonitis developed SIRS, highlighting the involvement of the systemic immune response.

The elevated proportion of band neutrophils observed in patients with SIRS likely reflects emergency granulopoiesis and rapid innate immune mobilization. In elderly patients, increased band forms may serve as a complementary marker to NLR and SII for identifying high-risk systemic inflammation and predicting postoperative complications.

Biomarkers, including CRP, WBC count, NLR, and SII, were elevated in patients with SIRS. This finding aligns with that of Liu et al. [36], who identified NLR and SII as reliable indicators of disease severity and outcomes in surgical infections. These biomarkers reflect neutrophil activation, lymphocyte suppression, and thrombocytosis, which are characteristic of systemic inflammation.

Research indicates that age-specific immunomodulatory treatments, including ozone therapy and lymphotropic antibiotics, can decrease complications and resolve inflammation faster. This is supported by evidence showing the benefits of immunocorrective therapy in managing inflammatory reactions while maintaining immune defenses. The SIRS group showed lower complication rates than the historical standards, suggesting protection.

In patients with SIRS, increased oxidative stress is shown through elevated WBC counts and CRP levels, supporting findings that link reactive oxygen species to immune disruption in older surgical patients [37]. Lipid peroxidation byproducts and enzymes have been linked to poorer outcomes in elderly patients with sepsis and SIRS [38,39].

This study emphasizes the importance of early SIRS identification in elderly patients with appendicitis. Due to altered immune parameters, standard markers may not accurately reflect the severity of inflammation. Incorporating geriatric assessments and composite indices, such as NLR and SII, is crucial, as recommended by geriatric surgery guidelines [40].

While surgery remains the primary treatment for appendicitis, immune support during the perioperative period is vital for high-risk groups. Immunocorrective strategies can reduce inflammation and improve outcomes. Our results indicate the need for prospective studies to confirm these protocols and investigate therapies targeting Toll-like receptor signaling and oxidative stress pathways [41–43].

Individuals with immunodeficiencies may exhibit diminished systemic inflammatory responses, making the traditional SIRS criteria less reliable for assessing severity. Among human immunodeficiency virus-positive patients with acute appendicitis, leukocytosis was lower (66.7% compared to 87%), and symptoms were more gradual, leading to delayed diagnosis and more complications [44]. Similarly, reviews have shown that immunocompromised individuals due to human immunodeficiency virus, cancer, chemotherapy, or immunosuppressive treatments often display altered clinical signs and laboratory results, making infection and sepsis detection more chal-

lenging [45,46]. Customized diagnostic approaches and studies to validate alternative biomarkers are necessary for these patient groups.

A significant correlation was found between SIRS and both age and disease severity. Patients in the elderly (61–74 years) and senile (≥ 75 years) age groups showed the highest incidence of SIRS, with 82.3% and 100% affected, respectively. The likelihood of meeting more SIRS criteria increased with age, as older individuals exhibited three or more symptoms of SIRS. SIRS prevalence differed based on appendicitis severity; it was uncommon in catarrhal cases but universal in gangrenous appendicitis with peritonitis. These results support the notion that both chronological age and histological disease stage independently predict systemic immune activation.

Further analysis of inflammatory markers reinforced the clinical stratification. Patients with SIRS showed higher WBC counts ($15.6 \pm 3.4 \times 10^9$cells/L) and CRP levels (84.3 ± 27.8 mg/L), along with elevated NLR and SII, which were linked to increased disease severity and worse outcomes. However, implementing an immunomodulatory perioperative protocol in the SIRS group was associated with decreased complications and quicker resolution of inflammation, as shown by the normalization of WBC counts and CRP levels within three days post-surgery. These findings highlight the advantages of targeted immune support strategies in enhancing postoperative recovery in elderly patients with SIRS following complicated appendicitis.

While early normalization of inflammatory markers such as WBC, CRP, NLR, SII, and band neutrophils by day 3–5 post-surgery indicates controlled inflammation, these markers alone cannot define recovery, particularly in older patients. A comprehensive evaluation must include complications, hospital stay duration, interventions, intensive care unit usage, 30-day outcomes, symptom resolution, and functional recovery. Thus, biomarker normalization should be considered supportive rather than conclusive evidence of recovery.

Direct assessment of cytokines such as IL-6, TNF-α, and IL-10 would provide mechanistic insights into immune dysregulation in elderly patients with appendicitis. Future prospective research should include cytokine panels and oxidative stress markers to enhance causal understanding, improve risk assessment, and inform immunomodulatory approaches for this vulnerable population.

5. Limitations

This study offers insights into the connection between acute appendicitis, SIRS, and immunosenescence in elderly patients. The retrospective nature of the study limits the ability to draw definitive causal conclusions. Although links were found between age, disease severity, inflammatory markers, and outcomes, the mechanisms remain speculative.

The single-center study in Kyrgyzstan limits its broader applicability. Differences in patient characteristics, comorbidities, surgical practices, and healthcare systems could affect the frequency and outcomes of SIRS in other studies. Excluding patients with prior abdominal surgeries or immunodeficiencies may not reflect real-world scenarios, particularly in older adults with multiple conditions.

Although standard SIRS criteria and biomarkers such as CRP, NLR, and SII were utilized, there was no advanced immunological profiling. The lack of cytokine panels, such as IL-6, TNF-α, and IL-10, along with oxidative stress markers such as malondialdehyde and myeloperoxidase, and functional immune assays, limited the understanding of systemic inflammation and immunosenescence in this group.

Monitoring of postoperative outcomes was limited to a hospitalization duration of up to five days. This may have led to an underestimation of later complications, readmissions, or ongoing immune dysfunction. Additionally, common comorbidities in older adults, such as diabetes, cardiovascular disease, and chronic kidney disease, were not systematically recorded or adjusted for, potentially causing residual confounding factors.

The perioperative immunocorrective protocol was implemented without randomization in the study. The lack of a parallel control group complicates attributing improved outcomes to this intervention, as other factors, such as surgery timing, antibiotics, and supportive care, might have played a role. To confirm these findings, future prospective multicenter randomized studies with extended follow-up and immunological evaluations are necessary.

6. Clinical Implications

This study has significant clinical implications for the treatment of acute appendicitis with SIRS, particularly in elderly patients. The link between age and both the occurrence and severity of SIRS highlights the need for increased

awareness and customized management plans for older individuals. Changes in immune function due to aging, such as immunosenescence and inflammaging, result in modified inflammatory responses, making traditional clinical signs less reliable in this population.

Since SIRS is common in elderly patients with severe appendicitis, particularly those with gangrenous peritonitis, prompt surgical intervention is essential. Delays in diagnosis or conservative treatment in high-risk elderly patients can lead to sepsis and organ failure in these patients. This study advocates for early surgical management in older patients with indicative symptoms, even in the absence of a typical inflammatory response.

The adoption of an immunocorrective perioperative protocol has shown promising results in decreasing complications, reducing inflammation, and accelerating recovery. This indicates that, alongside antibiotic treatment and surgical source control, immunomodulatory support could be valuable in managing high-risk patients. The use of ozonized saline lavage, lymphotropic antibiotic delivery, and immune-focused interventions addresses both microbial load and dysregulated immune responses.

This study emphasizes the importance of incorporating geriatric evaluations into surgical care and assessing function, nutrition, cognition, and frailty, which aids in preoperative risk evaluation and personalized care strategies. Elderly patients with SIRS represent a vulnerable group that benefits from multidisciplinary care involving surgeons, geriatricians, infectious disease experts, and critical care teams. Biomarkers such as CRP, NLR, and SII serve as diagnostic tools to track therapeutic responses and forecast outcomes.

7. Recommendations

Based on the results of this study, several clinical and research recommendations can be proposed to improve the diagnosis, treatment, and outcomes of elderly patients with acute appendicitis complicated by SIRS.

- Older and senile patients have a higher likelihood of developing SIRS and often show unusual symptoms. Healthcare providers should remain vigilant for signs of systemic inflammation, even in the absence of traditional indicators, such as fever or leukocytosis. The use of composite inflammatory indices, such as NLR and SII, improves early detection of SIRS in the elderly.
- Given the altered immunity in older patients, standardized age-specific immunomodulatory protocols are recommended perioperatively, including ozone lavage, lymphotropic antibiotics, and treatments to reduce inflammation. These targeted strategies have been linked to fewer complications and faster resolution of systemic inflammation in high-risk groups.
- Incorporating geriatric evaluations of functional capacity, frailty, cognition, and nutrition into the preoperative assessment of elderly patients with appendicitis is essential. This strategy helps determine the timing of surgery, postoperative care, and immune support needs, thereby enhancing patient safety and reducing complications.
- Regular monitoring of CRP, WBC count, NLR, and SII indicates whether systemic inflammation has resolved. If values remain high beyond 48 h, this may signal complications requiring closer observation. Standardization of postoperative monitoring protocols for these biomarkers is advisable, particularly in older adults.
- Although this retrospective study provides insights, larger multicenter prospective trials are needed to confirm the benefits of immunocorrective therapy and to understand the relationships between age-related immune changes and SIRS progression. Future research should include immunological profiling, cytokine measurements, and extended follow-up to comprehend the effects of aging on systemic inflammation in surgical patients.
- Managing elderly patients with SIRS requires the joint efforts of surgeons, anesthesiologists, geriatricians, and critical care teams. For older patients with complex appendicitis, a multidisciplinary approach ensures prompt intervention and optimal recovery outcomes.

8. Conclusion

This study reveals that frequency and intensity of SIRS rise with age in patients undergoing surgery for acute appendicitis. Older patients were more prone to multiple SIRS criteria, especially those with gangrenous appendicitis and peritonitis, highlighting the impact of immunosenescence and inflammaging.

SIRS was closely linked to increased inflammatory biomarkers, such as white blood cell count, C-reactive pro-

tein, neutrophil-to-lymphocyte ratio, and systemic immune-inflammation index, which were valuable for risk assessment. Patients receiving immunocorrective treatment during surgery experienced fewer complications and quicker normalization of immune markers, indicating that targeted immune modulation could enhance surgical outcomes in high-risk elderly groups.

These results emphasize the need for early detection of systemic inflammation, geriatric evaluations in perioperative planning, and consideration of immunomodulatory protocols. Future prospective multicenter studies, including cytokine profiling, oxidative stress markers, and long-term follow-up, are necessary to confirm these findings and improve strategies for managing acute appendicitis complicated by SIRS in older adults. Multicenter and international validation is needed to ensure that these single-center results are applicable across various healthcare environments.

Author Contributions

Conceptualization, S.A. and E.B.; methodology, A.A.; software, Y.V.; validation, A.A. and A.A.; formal analysis, Y.V.; investigation, S.A., E.B., A.A., and A.A.; data curation, R.O.; writing—original draft preparation, A.A., R.O., and Y.V.; writing—review and editing, Y.V. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

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Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

Data are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that there is no conflict of interest.

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