Identifying Factors Associated with Non-mesenterovascular Pathology in Patients Undergoing Surgical Treatment for Acute Mesenteric Ischemia

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Aim: To identify factors that can help us to avoid a preoperative incorrect diagnosis of vascular occlusion by evaluating patients who underwent laparotomy with a probable preoperative diagnosis of acute mesenteric ischemia (AMI), but later at laparotomy, were diagnosed to have a different pathology than AMI.

Material and Methods: A total of 213 patients who were operated with the diagnosis of AMI were enrolled in this study. Based on their operational, clinical, and pathological findings, they were divided into two groups. Patient demographic data, along with the American Society of Anesthesiology (ASA) score, Charlson comorbidity index, history of previous abdominal surgery, and computed tomography (CT) findings were compared between groups.

Results: There were 37 patients in Group 1 (non-mesenterovascular pathology) and 176 patients in Group 2 (mesenterovascular pathology). The percentage of ASA 4 patients was higher in Group 2, with 48.3%, compared to 35.1% in Group 1 (*p*-value: 0.028). Upon admission, Group 2 had a higher rate of pathologic findings on CT examinations. 21.8% of the patients with non-mesenterovascular pathology had normal intra-abdominal findings. In univariate and multivariate analysis for no-nmesenterovascular pathology, patient age less than 65, Charlson comorbidity index 1–2, INR level >1.2, history of previous abdominal operation, and pneumatosis intestinalis were identified as independent risk factors.

Discussion: The possibility of non-mesenterovascular pathology in presumed AMI patients should be kept in mind, especially if the patients have a history of abdominal surgery, a low comorbidity index, an elevated international normalised ratio (INR), and are younger than 65 years of age.

Conclusion: Evaluating the significant parameters identified in this study among patients with a preliminary diagnosis of AMI may prove useful in avoiding misdiagnosis and unnecessary surgeries.

Keywords: acute mesenteric ischemia; diagnosis; comorbidity

Introduction

Acute mesenteric ischemia (AMI) can be defined as an abrupt impairment of blood flow to a segment of the small intestine. AMI is not an isolated clinical entity; it is a complex of diseases, including acute mesenteric arterial embolism (50%) and thrombus (15–25%), mesenteric venous thrombus (5–15%), and non-occlusive mesenteric ischemia (20%) [1–3]. The overall incidence of AMI is low, but steadily increasing due to the rising number of patients with advanced age. It constitutes 0.09 to 0.2% of acute admissions to emergency services [1].

Despite the advances in radiology, it is still a challenging task to diagnose AMI early due to the lack of specific clinical and laboratory criteria. Many diseases that cause acute abdomen may mimic AMI, especially the presence of advanced age, hypercoagulability, arrhythmia, and heart valve disease, leading physicians to the misdiagnosis as AMI [4].

Mortality in AMI is high (50–80%) despite advances in diagnostic imaging modalities, surgical techniques, and intensive care support [1]. In the majority of cases, timely diagnosis cannot be made before bowel necrosis develops [5]. In AMI, which is mainly associated with embolism, the prognosis is significantly improved with early diagnosis and restoration of blood flow in the first 6 hours of ischemia. The prognosis worsens as the length of time of the intestinal ischemia increases [6]. Rapid diagnosis and intervention are essential to reduce high mortality rates. A 24-hour delay reduces the survival rate by at least 20% [2].

Many new diagnostic methods have been investigated in the literature to make an early diagnosis and thus reduce mortality [2, 6, 7]. Accurate diagnosis is as important as early diagnosis in mesenteric ischemia. Since AMI mainly affects the elderly patient group with comorbidities, unnec-

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Table 1. Demographic and clinical characteristics.

		Group 1	Group 2	*p*
		n(%)	n(%)	
Gender	Male	18 (48.6)	88 (50.0)	0.513
	Female	19 (51.4)	88 (50.0)	
Age (years)		61.43 ± 14.90 (25–88)	68.31 ± 13.00 (34–90)	0.005*
Charlson comorbidity index	0	0 (0.0)	1 (0.6)	0.038*
	1–2	15 (40.5)	34 (19.3)	
	3–4	20 (54.1)	134 (76.1)	
	≥5	2 (5.4)	7 (4.0)	
ASA score	1	1 (2.7)	0 (0.0)	0.028*
	2	6 (16.2)	12 (6.8)	
	3	17 (45.9)	79 (44.9)	
	4	13 (35.1)	85 (48.3)	
History of abdominal surgery	+	15 (40.5)	26 (14.8)	0.001*
	-	22 (59.5)	150 (85.2)	
Anticoagulan use	+	13 (35.1)	31 (17.6)	0.018*
	-	24 (64.9)	145 (82.4)	
History of malignancy	+	10 (27.0)	22 (12.5)	0.028*
	-	27 (73.0)	154 (87.5)	

ASA, American Society of Anesthesiology. The values marked with * are statistically significant values (< 0.05).

essary laparotomy for presumed mesenterovascular pathology will increase morbidity and mortality in this high-risk patient group.

Almost all of these suspected AMI patients undergo computed tomography (CT) examinations under emergency conditions. It is not always possible to find a qualified radiologist in emergency conditions, and it is often difficult to obtain a CT scan that meets the minimum requirements for proper imaging of these patients with poor general health and many additional medical conditions, such as renal failure or contrast allergy [8]. Therefore, to mitigate the risk of negative laparotomy, which is usually fatal in these patients, we aimed to identify parameters that can help us avoid incorrect preoperative diagnoses of vascular occlusion by evaluating patients who underwent laparotomy with a probable preoperative diagnosis of AMI, but later at laparotomy, were diagnosed to have a different pathology than AMI.

Materials and Methods

After the approval from the ethical committee, we included a total of 213 patients aged 18 years or older who underwent laparotomy with a preoperative diagnosis of AMI; patients with incomplete medical records or those who did not undergo laparotomy were excluded. Based on their operational, clinical, and pathological findings, they were divided into two groups: Group 1: patients with non-mesenterovascular pathology, and Group 2: patients with mesenterovascular pathology.

Patients' demographic data, along with American Society of Anesthesiology (ASA) score, Charlson comorbidity index, history of previous abdominal surgery, malignancy, anticoagulant use, physical examination, CT findings, and laboratory parameters measured at admission (white blood cell (WBC), C-reactive protein (CRP), procalcitonin erythrocyte sedimentation rate (ESR), Na^+, K^+, Lactate, D-dimer international normalized ratio (INR)) were compared between groups. Independent risk factors for non-mesenterovascular events were tested, with variables selected based on their clinical relevance and potential association with mesenterovascular pathology.

Statistical Analysis

We used SPSS (Statistical Package for the Social Sciences) 23.0 (IBM Corp., Armonk, NY, USA) for statistical analysis of the data. Categorical measurements were presented as number and percentage, and continuous measurements as mean and standard deviation (median and minimum-maximum where appropriate). The Pearson chi-square test was used to compare categorical variables. The Shapiro–Wilk test was used to determine whether the variables in the study adhered to a normal distribution. For comparison of continuous measurements between groups, Student's independent samples *t*-test was used for normally distributed variables, and the Mann–Whitney U test was used for non-normally distributed variables. Logistic regression analysis was applied to identify the independent variables that were

Table 2. Physical examination and laboratory measurements.

		Group 1	Group 2	*p*
		n(%)	n(%)	
Presence of abdominal tenderness	+	15 (40.5)	110 (62.5)	0.012*
	-	22 (59.5)	66 (37.5)	
Presence of abdominal distension	+	7 (18.9)	62 (35.2)	0.038*
	-	30 (81.1)	114 (64.8)	
WBC ($\times 10^9$/L)		12.51 ± 1.82 (8.1–18)	15.55 ± 4.04 (1.2–32)	0.001*
CRP (mg/L)		36.83 ± 36.92 (4–165)	43.68 ± 31.58 (5–222)	0.246
Procalcitonin (ng/mL)		0.80 ± 0.39 (0.23–1.54)	0.77 ± 0.98 (0.12–3.21)	0.739
NA^+ (mEq/L)		143.94 ± 3.89 (134–154)	142.13 ± 7.24 (128–167)	0.142
K^+ (mEq/L)		4.64 ± 0.44 (3.9–5.7)	4.53 ± 0.41 (3.9–5.7)	0.142
Lactate (mmol/L)		2.11 ± 0.79 (0.8–5)	2.44 ± 1.53 (0.5–21)	0.213
D-Dimer (mcg/mL)		1172.05 ± 976.21 (230–4500)	2099.77+1415.76 (289–7117)	0.001*
Sedimentation (mm/hr)		25.08 ± 15.95 (5–74)	27.39 ± 19.11 (2–98)	0.493
INR		1.85 ± 2.62 (0.8–13)	1.08 ± 0.29 (0.6–3.2)	0.001*

WBC, white blood cell; CRP, C-reactive protein; INR, international normalised ratio. The values marked with * are statistically significant values (< 0.05).

significant predictors of the dependent variable. The significance level was set at 0.05 in all tests.

Results

There were 37 patients in Group 1 (18 Female, 19 Male, age: 25–88 years, median: 61.43) and 176 patients in Group 2 (88 Female, 88 Male, age: 34–90, median: 68.31). Gender distribution was equally balanced within the groups. Mean age was significantly higher in Group 2 (*p*-value = 0,005). The patients in Group 2 had a higher mean charlson comorbidity index, and Group 2 had a higher percentage of ASA 4 patients. The prevalences of anticoagulant use and history of malignancy were higher in Group 1. Demographic and clinical characteristics of the patients are shown in Table 1.

With regard to physical examination findings, the presence of abdominal tenderness and distension were more prevalent in Group 2. Among laboratory parameters, WBC and D-dimer levels were higher in Group 2, and INR levels were higher in Group 1. CRP, procalcitonin, lactate, and ESR levels did not differ significantly between the groups. Physical examination findings and laboratory features are shown in Table 2.

CT examinations in the emergency department revealed higher prevalence of mesenteric stranding, intestinal wall thickening, and pneumatosis intestinalis in Group 2. Small bowel obstruction and the presence of intraabdominal free air and fluid did not differ significantly between the groups. Imaging findings are shown in Table 3.

In Group 1, more than half of the patients (20 patients) had unnecessary laparotomy due to medical causes. The negative laparotomy patients formed the most prevalent subgroup (8 patients) in Group 1 with regard to definitive postoperative diagnosis, followed by small bowel perforation (7 patients). The causes of non-mesenterovascular events are shown in Table 4.

In univariate and multivariate analyses for prediction of non-mesenterovascular pathology (Group 1), patient age less than 65 years, Charlson comorbidity index of 1–2, INR levels higher than 1.2, ASA score less than 3, previous abdominal surgery, history of malignancy, and absence of abdominal tenderness, intestinal wall thickening, mesenteric stranding, and pneumatosis intestinalis were identified as independent risk factors (Table 5).

Table 3. Preoperative Imaging findings.

		Group 1	Group 2	*p*
		n(%)	n(%)	
Mesenteric stranding	+	18 (48.6)	141 (80.1)	0.001*
	-	19 (51.4)	35 (19.9)	
Small bowel obstruction	+	6 (16.2)	33 (18.8)	0.462
	-	31 (83.8)	143 (81.2)	
Intestinal wall thickening	+	18 (48.6)	126 (71.6)	0.007*
	-	19 (51.4)	50 (28.4)	
Free intaabdominal air	+	10 (27.0)	40 (22.7)	0.356
	-	27 (73.0)	136 (77.3)	
Free intraabdominal fluid	+	13 (35.1)	72 (40.9)	0.323
	-	24 (64.9)	104 (59.1)	
Pneumatosis intestinalis	+	4 (10.8)	77 (43.8)	0.001*
	-	33 (89.2)	99 (56.2)	

The values marked with * are statistically significant values (< 0.05).

Table 4. Non-mesenterovascular findings.

Variable	N
Normal Intra-Abdominal Findings	8
Small Bowel Perforation	7
Peptic Ulcer Perforation	4
Perforated Appendicitis	2
Inflammatory Bowel Disease	2
Acute Cholecystitis	2
Mesenteric lymphadenopathy	2
Intestinal Obstruction	4
Tumor Perforation in the Sigmoid Colon	1
Left Salpingo oophoritis	1
Mural Hematoma	1
Tuberculous Peritonitis	1
Retroperitoneal Hematoma	1
Basal Lobe Pneumonia	2

Discussion

Despite the improvements in surgical techniques, interventional radiology, and intensive care unit capabilities, AMI continues to have a high mortality rate. The main reasons for this high mortality rate are the difficulty and delay in diagnosis before intestinal necrosis develops. The literature generally agrees that early diagnosis and prompt and proper management are the mainstays of a favorable outcome [9]. For this reason, when dealing with patients with abdominal pain, physicians generally keep in mind the possibility of AMI diagnosis, especially in patients who have acute abdominal pain not consistent with physical examination. However, these patients are almost always elderly and have more than one severe comorbidity [10]. Therefore, the treatment strategy must not involve unnecessary interventional procedures, especially surgery, as these may have catastrophic outcomes. Our study addresses an important gap in the literature by evaluating several patient characteristics as predictors of non-mesenterovascular pathology, in order to help avoid misdiagnosis of AMI. Although many studies have examined the efficacy of laboratory tests and radiologic investigations in the diagnosis of AMI, almost all of them concluded that the lack of a single diagnostic parameter is an important ongoing problem [11]. Additionally, there are many conflicting reports about the usefulness of commonly included parameters like D-dimer, WBC, and lactate levels [12]. In the literature, radiologic investigations are considered to be more accurate in the diagnosis of AMI; however, their dependence on contrast and possible allergic reactions greatly limits their routine usage, which often leads to diagnosis based on secondary findings rather than direct visualization of the vasculature [13, 14]. Moreover, in almost all of these patients, the imaging is done under emergency conditions that render optimal imaging difficult due to the potential lack of technical sufficiency, like modern equipment, experienced technicians, and patient compatibility.

Table 5. Univariate and multivariate analysis of factors associated with non-mesenterovascular pathology.

Measurements		Univariate	Multivariate	
		p	HR (95%CI)	*p*
Age (years)	≥65	0.001*	1.000	0.001*
	<65		4.026 (1.928–8.407)	
Sex	Female	0.880	1.000	0.881
	Male		1.056 (0.519–2.145)	
Charlson comorbidity index	≥3	0.010*	1.000	0.009*
	1–2		0.364 (0.171–0.773)	
ASA score	≥3	0.032*	1.000	0.024*
	1–2		3.189 (1.161–8.757)	
WBC ($\times 10^9$/L)	≤4	0.081	1.000	0.080
	≥10		0.758 (0.324–1.124)	0.436
	4 < WBC < 10		0.650 (0.475–0.825)	0.995
D-dimer (mcg/mL)	>500	0.166	1.000	0.143
	<500		3.018 (0.688–13.229)	
INR	<1.2	0.001*	1.000	0.001*
	≥1.2		0.255 (0.122–0.535)	
History of abdominal surgery		0.001*	3.976 (1.804–8.765)	0.001*
History of malignancy		0.025*	2.642 (1.087–6.419)	0.032*
Absence of abdominal tenderness		0.001*	0.273 (0.130–0.575)	0.001*
Absence of abdominal distention		0.045*	0.429 (0.178–1.033)	0.059
Absence of mesenteric stranding		0.001*	0.235 (0.112–0.495)	0.001*
Absence of bowel wall thickening		0.008*	0.376 (0.182–0.775)	0.008*
Absence of pneumatosis intestinalis		0.001*	0.156 (0.053–0.459)	0.001*

The values marked with * are statistically significant values (< 0.05).

Abdominal pain varies widely among patients, ranging from mild pain to severe abdominal pain. In addition, physical examination findings may vary. The situation described as "abdominal pain inconsistent with advanced age and physical examination" in surgical practice should bring to mind AMI. However, this classic presentation may not be present in 20–25% of patients with AMI [15]. In our study, we found that abdominal tenderness and distension were more frequently observed in patients with mesenterovascular events. This highlights the importance of physical examination findings for diagnosis of AMI.

In suspected AMI patients, to get an early diagnosis and proper treatment algorithm, the physician must take into consideration many possible parameters such as physical, laboratory, and radiologic findings, vital parameters, medical history, and comorbidities of the patients. Additionally, they must come to a correct conclusion quickly, because in the case of AMI, delay in diagnosis increases the risk of intestinal ischemia and eventually necrosis, which is the main cause of the high rate of complications and mortality [16–18].

Of 213 patients operated in emergency conditions with a preoperative diagnosis of AMI, 37 (17%) had a different postoperative diagnosis; of those, 20 (54%) had a negative laparotomy or a medical pathology. Treatment of a medical pathology by surgery, especially in this subgroup of elderly and comorbid patients, increases the risk of significant complications, even death. Technological advances and increased expertise may help us to diagnose these patients appropriately. In multivariate analysis, young age, low comorbidity index, previous abdominal surgery, history of malignancy, anticoagulant use, low D-dimer, high INR levels, lack of intestinal wall thickening, and pneumatosis intestinalis on CT were found to be significant predictors of non-mesenterovascular pathology. For the physicians that seek to find a correct diagnosis, these factors may suggest that the underlying pathology of acute abdomen may not be AMI. With regard to these significant parameters, it is evident that an emergency center dealing with this group of patients not only requires experienced physicians but also requires qualified radiologists and standardized laboratory and radiology units open 24/7. Once these criteria are met, one might hope to decrease the rate of patients unnecessarily operated in presumed AMI patients.

Conclusion

Acute mesenteric ischemia is still difficult to treat because of the high death rate from misdiagnosis or delayed treat-

ment. Positive outcomes depend on early detection and timely care; yet, diagnosis can be challenging due to the complexity of clinical presentation, particularly in older patients with numerous comorbidities. In order to avoid misdiagnosis and needless surgical procedures, our study highlights the significance of an all-encompassing strategy that incorporates clinical, laboratory, and radiographic criteria, especially in patients with non-mesenterovascular pathology. Through the identification of critical variables including age, comorbidity index, medical history, and radiological results, we provide insightful information to support doctors in improving their diagnostic proficiency. Moreover, our results support the improvement of emergency care environments by providing 24-hour access to skilled medical personnel and state-of-the-art diagnostic facilities. Our ultimate goal is to lessen the burden of incorrect diagnoses and improve the general management of patients who present with severe abdominal pain suggestive of AMI by utilizing technology breakthroughs and interdisciplinary teamwork.

Availability of Data and Materials

The author will supply the relevant data in response to reasonable requests.

Author Contributions

FD and TT conceptualized the study and contributed to data analysis. MA and EMS conducted literature review and drafted the manuscript. FD, HYA, MA and MK collected and analyzed the data. EMS contributed to study design and interpretation of results. MK provided critical revisions and final approval of the manuscript. HYA supervised the research project. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Ethical approval of our study was obtained from the Erciyes University Ethics Committee on 20.05.2020, decision number 2020/249. Informed patient consent was obtained for this study in accordance with the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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