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ORIGINAL ARTICLE

Midterm renal functions following acute renal infarction

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Abstract The aim of this study was to explore clinical features of renal infarction (RI) that may have a role in diagnosis and treatment in our patient cohort and provide data on midterm renal functions. Medical records of patients with diagnosis of acute RI, established by contrast enhanced computed tomography (CT) and at least 1 year follow-up data, who were hospitalized in our clinic between 1998 and 2012 were retrospectively reviewed; including descriptive data, clinical signs and symptoms, etiologic factors, laboratory findings, and prescribed treatments. Patients with solitary infarct were treated with acetylsalicylic acid (ASA) only, whereas patients with atrial fibrillation (AF) or multiple or global infarct were treated with anticoagulants. Estimated Glomerular Filtration Rate (eGFR) referring to renal functions was determined by the Modification of Diet in Renal Disease (MDRD) formula. Twenty-seven renal units of 23 patients with acute RI were identified. The mean age was 59.7 ± 15.7 years. Fourteen patients (60.8%) with RI had atrial fibrillation (AF) as an etiologic factor of which four had concomitant mesenteric ischemia at diagnosis. At presentation, 20 patients (86.9%) had elevated serum lactate dehydrogenase (LDH), 18 patients (78.2%) had leukocytosis, and 16 patients (69.5%) had microscopic hematuria. Two patients with concomitant mesenteric ischemia and AF passed away during follow up. Mean eGFR was 70.8 ± 23.2 mL/min/1.73 m^2 at admission and increased to 82.3 ± 23.4 mL/min/1.73 m^2 at 1 year follow up. RI should be considered in patients with persistent flank or abdominal pain, particularly if they are at high risk of thromboembolism. Antiplatelet and/or anticoagulant drugs are both effective treatment options according to the amplitude of the infarct for preserving kidney functions.

Conflicts of interest: All authors declare no conflicts of interest.

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Introduction

Renal infarction (RI) is usually misdiagnosed at the initial presentation of patients because of its rarity, so high suspicion is of utmost importance for early diagnosis. It is often mimicked by other more common conditions such as urolithiasis, lower back pain caused by lumbar disc hernia or spinal stenosis, and acute abdomen. Incidence of RI was reported as four to seven cases in 100,000 of emergency department visits [1,2]. Most common causes of RI are traumatic, thromboembolic, atheroembolic, and thrombotic conditions [2]. Most of the published articles on this topic are mainly based on case series [1,3—5]. Some laboratory parameters such as elevated serum lactate dehydrogenase (LDH) levels, microscopic hematuria and impaired renal functions described by elevated serum creatinine levels are the most encountered findings accompanying acute abdominal or flank pain in one of the largest series reported by Hazanov et al [5]. Considering diagnostic imaging, contrast-enhanced computed tomography (CT) seems the most appropriate method for evaluating patients suspected of having RI, furthermore renal isotope scans or renal angiography may help in doubtful cases [1—3,5]. Thrombolytic, anticoagulant and antiaggregant therapies have been used in previous reports [1—5]. Despite absence of clear-cut recommendations for management of the condition, it is not anticipated to be discrete from the common approach to thromboembolic events. The above-mentioned studies mainly focus on diagnostic scheme and acute management of these patients whereas detailed long-term follow-up data regarding renal functions are missing in most series. Thus, we aimed to evaluate the diagnostic and therapeutic management of patients and provide data especially on mid-term renal functions of patients who were hospitalized in our clinic with acute RI.

Methods

Medical records of all patients who were hospitalized and treated in our department with the definitive diagnosis of acute RI confirmed by CT and with at least 1 year follow-up data between 1998 and 2012 were retrospectively reviewed. We diagnosed RI on the basis of CT scan appearance. A renal infarct was defined as a peripheral triangle-shaped area in the renal parenchyma which was slightly hypodense on unenhanced scans using predefined display window settings for soft tissues [20—40 Hounsfield units (HU)], and which showed no contrast enhancement [6]. Descriptive data, medical history, comorbid conditions, clinical signs and symptoms, complete blood count (CBC), biochemical analysis, urinalysis, and CT findings at admission were evaluated. In our institution, 100 mg acetylsalicylic acid (ASA) is used to treat solitary infarcts in those without atrial fibrillation (AF). We use intravenous or subcutaneous heparin followed by oral warfarin to treat patients with bilateral, multiple, or global infarcts and those with AF.

Estimated Glomerular filtration rate (eGFR) was calculated according to the Modification of Diet in Renal Disease (MDRD) formula both at admission and also at 1 month and 1 year follow up [7]. Data were analyzed using descriptive statistics.

Results

A total of 23 patients (12 male) were included in the study. Their mean age was 59.7 ± 15.7 years. Their body mass index was 29.5 ± 5.4 kg/m^2. Further details of characteristics and clinical manifestations of patients are given in Table 1. At presentation, 14 patients (61%) had AF, 12 patients (52%) had hypertension, and four patients (17%) had mesenteric ischemia. At the time of admission, 13 patients (56.5%) had abdominal pain and 10 patients (43.4%) had flank pain. In addition to abdominal or flank pain, seven individuals (30.4%) reported nausea, and five individuals (21.7%) had vomited. On examination, 18 patients (78.2%) had abdominal tenderness, 11 patients (47.8%) had costovertebral tenderness, and three patients (13%) were febrile.

By CT scan, left kidney RI was diagnosed in 10 patients (43.4%), right kidney RI in nine patients (39.1%) and bilateral RI in four patients (17.3%). Consequently, a total of 27 kidneys had areas of RI. Ten kidneys (37%) had a solitary area of infarction (Figure 1), eight kidneys (29.6%) had multiple areas of infarction (Figure 2), and nine kidneys (33.3%) were globally infarcted. Elevated LDH levels were the most frequent abnormal finding in 73.9% of patients at admission and in 86.9% of patients 24 hours after admission. Detailed analyses of laboratory findings are provided in Table 2. Fourteen patients had atrial fibrillation (AF); 12 patients had hypertension, and four patients had concomitant mesenteric ischemia at diagnosis. Among these patients with AF, 11 of them had multiple infarcts or global infarction of kidney. Considering the four patients with concomitant mesenteric ischemia; three of them had bilateral RI and two of them passed away during the following month. The first patient who passed away was a 69-year-old male who presented with abdominal pain, nausea, and vomiting. He had abdominal tenderness on physical examination, his eGFR was 55 mL/min/1.73 m^2, and he had AF. He expired on the 4th day of his hospitalization. The second patient who passed away was a 66-year-

Table 1 Characteristics and clinical manifestations of patients with renal infarction.

Characteristics and clinical manifestation	
Age (y)	59.7 ± 15.7
Male/female	12/11
Body mass index (kg/m^2)	29.5 ± 5.4
Abdominal pain	13 (56.5)
Flank pain	10 (43.4)
Nausea	7 (30.4)
Vomiting	5 (21.7)
Abdominal tenderness	18 (78.2)
Fever	3 (13.0)
Costovertebral angle tenderness	11 (47.8)

Data are presented as *n* (%) or mean ± SD, unless otherwise indicated.

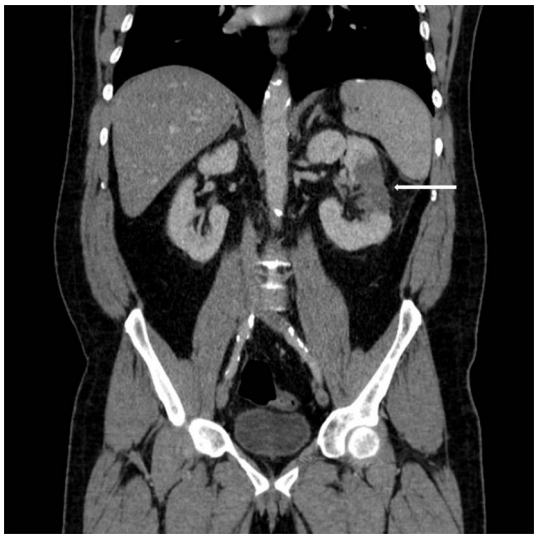

Figure 1. A solitary infarct in the left kidney (indicated by arrow).

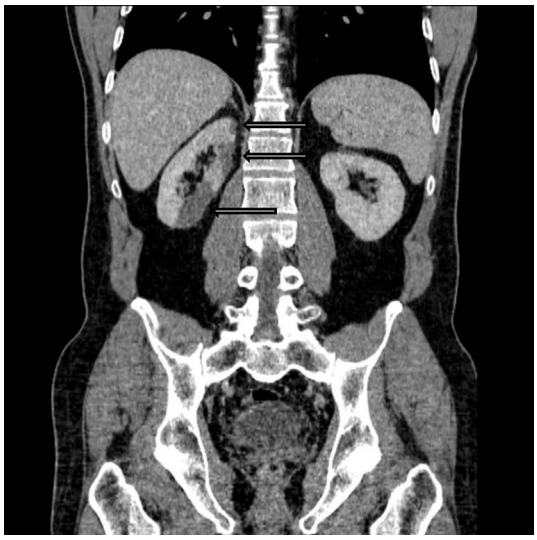

Figure 2. Multiple infarctions in the right kidney (indicated by arrows).

old male, he also presented with abdominal pain, nausea, and vomiting. He had abdominal tenderness on physical examination, his eGFR was 81 mL/min/1.73 m^2, and he expired on the 3rd day of his hospitalization. None of the patients with solitary infarct (5/23) had impaired renal function on admission. Their mean age was 43.8 $\pm$ 13.1 years. The mean age of the 18 patients with AF and bilateral infarcts, multiple infarcts, or global infarction was 64.1 $\pm$ 13.5 years. Eight of them had impaired renal function (eGFR $<$ 60 mL/min/1.73 m^2) at admission. eGFR increased above 60 mL/min/1.73 m^2 in three patients with impaired renal function at 1 month follow up. Five patients remained with impaired renal function at 1 month and 1 year follow up, however no requirement of dialysis was indicated for these patients. The mean age of these five patients, three of them female, was 75 $\pm$ 9.1 years; body mass index (BMI) was 33.6 $\pm$ 4.9 kg/m^2. Four of them presented with abdominal pain, one with flank pain; and one felt nausea. All had abdominal tenderness. All of the five patients with remaining impaired renal function had elevated LDH, creatine kinase (CK) and alkaline phosphatase (ALP) on admission; three of the five had an elevated white blood cell count (WBC), four of them had elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) at admission.

Discussion

We shared our 15 years' experience with 23 RI patients treated in our clinic. Abdominal or flank pain are the most frequent symptoms and are usually accompanied by vomiting, nausea, and fever [3]. All of the patients in our series also had abdominal or flank pain. After the elimination of the most common diseases with this presentation, RI should be remembered in the differential diagnosis. RI occurred at almost the same ratio between the right and left kidney (39–43%) in our patient cohort. It has been postulated previously that RI occurs in the left kidney more often because of the fact that the left renal artery forms an acute angle with the aorta [8]. However more recent case series also report that occurrence rates for left and right kidney are similar [9].

Serum LDH elevation is a marker for cell necrosis and LDH levels remain high ~15 days after the start of the

Table 2 Laboratory findings of patients hospitalized with the diagnosis of acute renal infarction.

Laboratory data (normal ranges)	Rate of elevation at admission, *n* (%)	Rate of elevation 24 h after admission, *n* (%)	Median levels at admission	Median levels 24 h after admission
LDH (125–243 U/L)	17/23 (73.9)	20/23 (86.9)	691 (210–1050)	958 (508–1523)
WBC (4–10 $10^3/\mu L$)	15/23 (65.2)	18/23 (78.2)	12.9 (8.7–17.2)	13.5 (12.1–16.9)
CK (29–168 U/L)	8/23 (34.7)	14/23 (60.8)	47 (28–77)	296 (52–639)
AST (5–34 U/L)	14/23 (60.8)	16/23 (69.5)	35 (25–52)	47 (28–77)
ALT (0–55 U/L)	8/23 (34.7)	9/23 (39.1)	44 (21–68)	45 (23–77)
ALP (40–150 U/L)	8/23 (34.7)	10/23 (43.4)	99 (82–189)	108 (86–200)
CRE (0.6–1.1 mg/dL)	7/23 (30.4)	7/23 (30.4)	0.95 (0.83–1.20)	0.95 (0.84–1.22)
Hematuria (>3)	12/23 (52.1)	16/23 (69.5)	—	—

ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CK = creatinine kinase; CRE = serum creatinine; LDH = lactate dehydrogenase; WBC = white blood cell count.

symptoms in patients with RI [9]. If there is a high clinical suspicion of acute RI, serum LDH should be repeated 24 hours after admission since normal values at admission may increase, as in our patient cohort. Patients with RI have hematuria (54—100%) and elevated LDH [5,10]. Over 80% of the patients with RI have pain, elevated LDH, and proteinuria and/or hematuria [3]. In our series 86.9% of patients had elevated LDH and 69.5% of patients had hematuria. 65% of them had pain, elevated LDH, and hematuria. Serum LDH is strongly suggestive of RI but we know that it cannot make an accurate diagnosis for RI. Contrast-enhanced CT is still the gold standard for the diagnosis of RI [6]. We believe that serum LDH may help to consider RI in differential diagnosis and lead to a further evaluation with contrast-enhanced CT.

Most patients with RI have a high risk history of thromboembolism. It was noted in the literature that most patients with RI had AF, hypertension, valvular disease, ischemic heart disease, or coagulation abnormalities, suggesting at least one thromboembolic risk factor [5]. AF and hypertension were also found to be the most frequent risk factors for RI in our patients concordant with previous reports.

Acute mesenteric ischemia is usually lethal and has high mortality rates of ~60—80% [11]. The majority of cases are misdiagnosed because the role of current radiographic and noninvasive modalities is limited in the early diagnosis of acute mesenteric ischemia. CT scans may reveal bowel wall thickening, ascites, or occlusion of the mesenteric arterial trunk. But, those signs are nonspecific and usually found only in the late stage of mesenteric ischemia [12]. Two out of four patients with concomitant mesenteric ischemia passed away during the 1 month follow up in our patient cohort. Three of them had bilateral RI. Because of the high mortality of mesenteric ischemia, if clinical signs of mesenteric ischemia are found after the diagnosis of RI, further investigation should be carried out. As seen in our series, determination of concomitant mesenteric ischemia has usually been accompanied by bilateral renal infarction. Mesenteric ischemia should be kept in mind if the patient has bilateral RI.

No proven therapeutic guidelines for the treatment of RI have been established. The therapeutic options include medical therapy and operative revascularization. Previous studies have shown that medical therapy is as effective as surgical therapy [8,13,14]. Medical therapy can be intra-arterial thrombolytic therapy, anticoagulation, and ASA [3,5,10]. However, these options depend on the duration of symptoms. Thrombolytic therapy was found to be better if used within 90—180 minutes while the renal tissue is still viable, but nearly all diagnoses of RI are made after the first 24 hours [9]. Early diagnosis enables more effective therapeutic intervention. In the cases presented here, the patients who had AF, global infarction, multiple infarctions, or bilateral infarction were treated with low molecular weight heparin or intravenous heparin and warfarin to bring their anticoagulation into the therapeutic range. The patients with solitary infarct in the kidney and with no AF were treated with 100 mg of oral ASA. In addition, because these patients are also at a high risk for further thromboembolisms, long-term anticoagulation is mandatory. No additional thromboembolic event was seen in our patients.

Regarding studies reporting evaluation of renal functions on follow up, Huang et al [3] gave the 1 year follow up of four patients with impaired renal function at admission, concluding that none of those patients required dialysis. Twenty percent of their patients had impaired renal function at admission which is lower than our 34.7% rate. However, they do not provide detailed information about renal functions. A more recent report by Bourgault et al [9], which has been the largest case series on this topic to date ($n = 94$), mentioned that 40.4% (38/94) of the patients had impaired renal functions of whom seven required hemodialysis at initial presentation and three developed end stage renal disease. No patient required dialysis in our cohort at admission or at 1 year follow up. In a recent study Bae et al [15] presented the effects of RI on renal functions and most of the patients recovered spontaneously. Our study is the first providing data regarding midterm renal functions for the Turkish patient population. We demonstrate that renal functions continue to heal in all patients with renal infarct under antiplatelet and anticoagulant therapies through 1 year follow up.

Our study had several important limitations. First, it was a retrospective study using a database and the medical records of the patients; only patients with available results were enrolled. Second, the number of the patients with RI was limited. Furthermore; clinical approach, availability of diagnosis, and treatment options as well as clinical awareness of the disease may vary over 15 years.

A high index of clinical suspicion is needed and this is the key of early diagnosis; RI should be taken into consideration for differential diagnosis in patients with a high risk of thromboembolism, persistent flank or abdominal pain, elevated serum LDH, and hematuria. Contrast-enhanced CT should be performed immediately to demonstrate or rule out RI. If patients have AF and bilateral RI, there might be an increased risk of concomitant mesenteric ischemia. Patients with solitary infarct in the kidney and with no AF can be safely treated with 100 mg ASA to prevent recurrent thromboembolic events and preserve renal functions.

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