

RENAL ARTERY THROMBOEMBOLISM: AN UNRECOGNIZED CAUSE OF ACUTE RENAL FAILURE

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SUMMARY – Acute renal artery thromboembolism is a critical condition and significant but commonly misdiagnosed and possibly reversible cause of kidney ischemic disease. This disorder is commonly overlooked, and an early and proper diagnosis can lead to proper therapy with greater chance for recovery of renal function and avoidance of unnecessary invasive diagnostic and therapeutic procedures. When encountering a patient suffering from acute renal failure and atypical lower back or abdominal pain, especially one who has high risk factors, we recommend diagnostic screening based on serum lactate dehydrogenase determination with other diagnostic procedures and therapeutic algorithm for renal artery thromboembolism.

Key words: *Renal artery obstruction – diagnosis; Renal artery obstruction – complications; Kidney failure, acute – etiology; Kidney failure, acute – drug therapy; Thromboembolism – complications*

Introduction

Renal artery thromboembolism (RATE) is an infrequent but significant cause of renal mass and renal function loss. Renal arteries are end-arteries and acute occlusion always results in an infarction. In fully established cases, the pathology is that of renal infarction, the extent of which is determined by the size of the thrombus and the vessel or vessels occluded. The major causes of renal infarction include emboli secondary to cardiac disease such as valvular heart disease, atherosclerosis, postinfarction left ventricular aneurysm with intra-aneurysmal thrombus, ventricular or interatrial septal aneurysms, interatrial or interventricular septal defect, bacterial endocarditis, heart tumors, and dilated cardiomyopathy. Particularly, atrial fibrillation either rheumatic or nonrheumatic, increases the risk of RATE¹⁻⁴. If RATE is not suspected, the diagnosis is difficult and unilateral thromboembolic occlusion may go undetected or may be detected too late. Therefore, the

real incidence of RATE is probably underestimated. The incidence of renal artery occlusion (non-thromboembolic) rises in cases associated with numerous risk factors. The etiologic factors for RATE include congenital crossed fused renal ectopia-horseshoe kidney⁵, trauma⁶, polycystic kidney disease⁷, polycythemia rubra vera, nephritic syndrome⁸, factor V Leiden mutation⁹, fibromuscular dysplasia, extra-adrenal pheochromocytoma, dissection of aorta or renal artery, and after manipulation of the aorta or other large arteries during arteriography, angioplasty, or surgery¹⁰. They can also occur spontaneously or after treatment with heparin, warfarin, or thrombolytic agents¹¹. Moreover, renal infarctions have been reported in patients with connective tissue diseases such as systemic lupus erythematosus, primary antiphospholipid antibody syndrome, polyarteritis nodosa, systemic vasculitis, mixed connective tissue disease, and Behcet's disease¹². Renal arterial abnormalities may be due to thrombosis associated with umbilical artery catheter placement in the newborn. Thrombi that form on the tip or surface of the catheter can partially or completely occlude abdominal aorta, thereby decreasing renal perfusion. These thrombi may also produce emboli to renal artery, resulting in areas of infarction and increased renin release. Renal arterial thrombosis is a rare cause of acute

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renal failure related to the use of angiotensin converting enzyme inhibitors (ACEi). This complication appears to occur most often in patients with marked (>95%) stenotic lesion who have an excessive reduction in blood pressure. It is therefore unclear if there is any specific predisposing effect of ACEi.

When Should RATE Be Suspected?

The clinical features of renal artery occlusion are quite variable. A high degree of suspicion is a prerequisite for diagnosing acute RATE in patients who present with unexplained abdominal/flank/lower back pain and acute renal failure. Most of the patients have a history associated with a high risk of thromboembolism. The complete occlusion of kidney arterial blood supply leads to segmental or total renal infarction. In this setting, the patient typically complains of the acute onset of nausea, vomiting, flank or abdominal pain and tenderness, and fever. These complaints may be accompanied by a significant elevation in blood pressure that is presumably renin-mediated. Acute mesenteric thromboembolism must be considered on differential diagnosis. Sometimes it may happen together with renal embolism and generally produces the acute abdomen symptoms³. Haematuria is present in up to 40% of patients and anuria can be present when the occlusion is bilateral or in a solitary kidney. Signs of extrarenal embolization (i.e. skin lesions or focal neurogenic deficits) may also be present. The alteration of mental state¹³ and hypertensive crisis¹⁴ are rare presentations of RATE.

Diagnostic Tests

Routine laboratory tests are often not helpful. Laboratory signs of renal insufficiency can only be found in patients suffering from bilateral RATE or in those with unilateral RATE in which the contralateral kidney is non-functional, has been surgically removed, or in patients with congenital solitary kidney. Elevation of serum creatinine may be found in patients with unilateral RATE and previous chronic renal failure. In the appropriate clinical setting, a markedly elevated serum lactate dehydrogenase (LDH) level (often more than 5-fold), with little or no rise in serum transaminases, are strongly suggestive of renal infarction¹⁵. Measurement of urinary LDH excretion may also be helpful. This enzyme is too large to be filtered and therefore its excretion rate is normal in extrarenal disorders, but elevated in renal infarction and transplant rejection. The prevalence of slight elevation of serum aspartate

aminotransferase (AST), amino alanintransferase (ALT) and alkaline phosphatase (AP) is 60%-70%, 50%-60% and 30%-40%, respectively¹⁶. Gross or microscopic hematuria is seen in approximately 30% of patients. Absence of hematuria reflects marked reduction of blood flow to the infarcted area, resulting in local cessation of glomerular filtration and urine flow.

Radioisotope renogram is the diagnostic procedure of choice to demonstrate a segmental or generalized decrease in renal perfusion. This procedure is noninvasive and often obviates the need for renal arteriography or contrast-enhanced computed tomography (CT) scanning.

Intravenous urography (IVU) classically shows no apparent kidney, although a cortical rim can sometimes be seen, suggesting actual existence of collateral circulation. The apparent absence of the kidney on IVU may be caused by RATE or severe spasm of the renal artery¹⁷. Occasionally, contrast nephropathy following IVU may itself lead to impairment of renal function and should be avoided.

Ultrasonography alone is of little use in detecting RATE, but it can be helpful in confirming the presence or absence of a kidney, and to exclude nephrolithiasis. However, when combined with renal power Doppler analysis using a duplex scanner, ultrasonography can be used to diagnose occluded renal arteries when the kidney is >8.5 cm long and there is no signal. However, the results are dependent on the operator¹⁸.

Contrast-enhanced CT of the abdomen is indicated when other injuries are suspected or the results of IVU are inconclusive¹⁹. Contrast-enhanced CT shows an area of decreased accentuation and a thin rim of cortical accentuation, but the use of intravenous contrast material is required.

Transfemoral renal arterial angiography offers the best sensitivity but contrast nephropathy following angiography may itself lead to acute renal failure.

Transthoracic or transesophageal echocardiography is used to evaluate the presence of cardiac thrombi responsible for embolism.

Electrocardiography is used to detect cardiac dysrhythmias.

Although transfemoral renal arteriography performed early seems to offer the best diagnostic sensitivity, renal power Doppler, renal scintigraphy and contrast-enhanced CT have also been found useful.

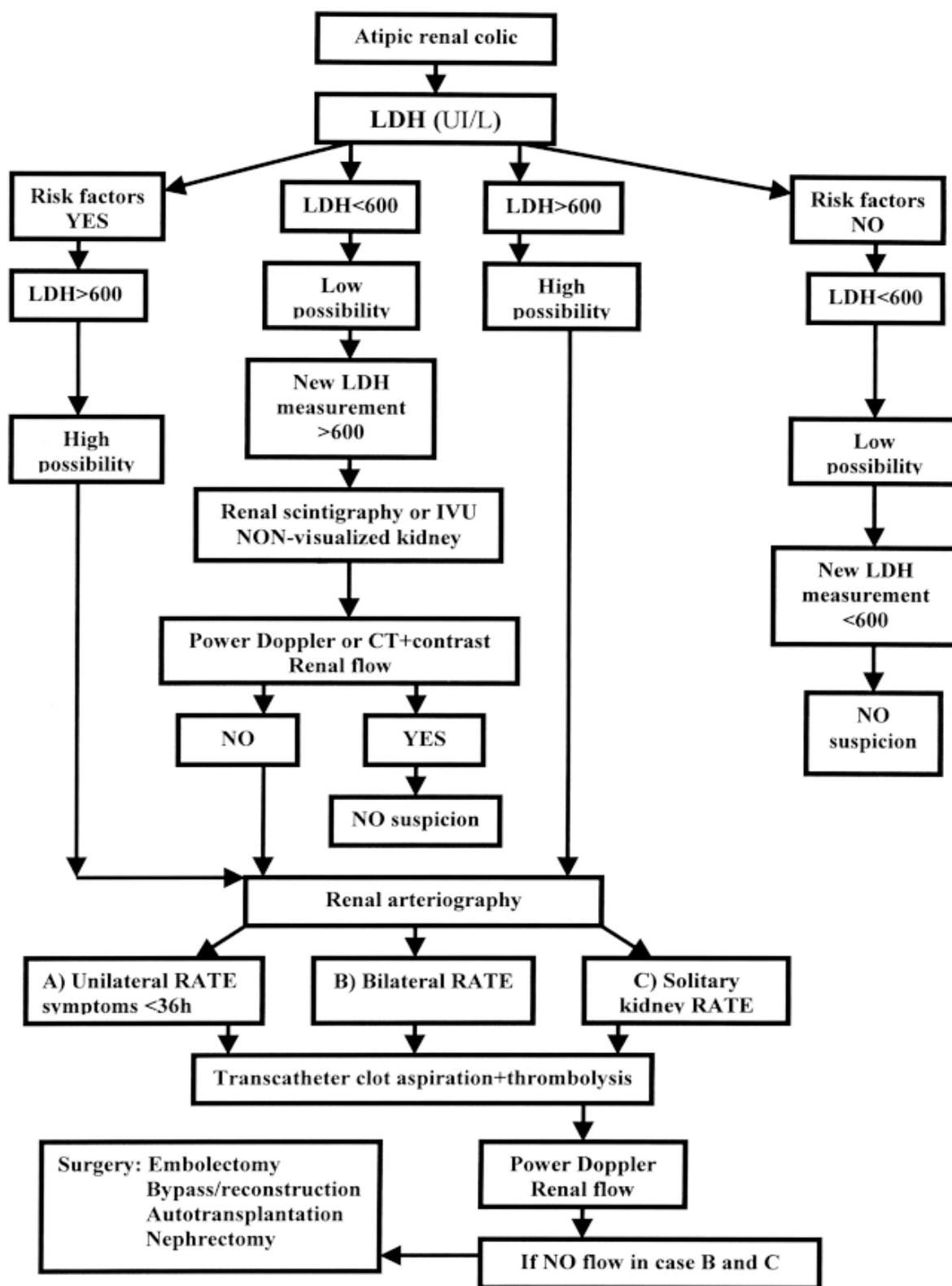


Fig. 1. Algorithm for diagnosis and treatment of renal artery thromboembolism (RATE)

Treatment Strategy

The optimal treatment for kidney infarction due to clot emboli is uncertain. Early surgery (within the first few hours) may restore vascular potency, but it is associated with high mortality rate and with no better renal functional recovery than that seen with anticoagulation or thromboembolic therapy alone.

Early diagnosis and treatment are compulsory to restore renal function and to avoid end-stage renal disease and chronic dialysis. The duration of ischemia is an important factor for recovering renal function. Infarction of the native kidney *in situ* occurs after <8 h of warm ischemia, however, successful late revascularization has also been reported²⁰. Preserved vascularization either by incomplete obstruction or by collateral circulation *via* peripelvic, periureteric and capsular branches enables the ischemic kidney to restore its renal output when renal artery flow is re-established and tubular lesions have healed. Re-establishing the blood flow to occluded kidneys should be attempted without regard to strict time-frames²¹.

Prompt treatment of the acutely occluded renal artery is emphasized by all authors. Several authors favor surgical embolectomy whenever embolus occurs at the main renal artery in bilateral or unilateral embolism with a solitary functional kidney²². Arteriotomy of the renal artery is carried out, followed by embolus extraction and evaluation of blood back flow. Finally, intra-arterial flushing with a solution of serum saline containing 100,000 units of Urokinase is recommended. Whenever possible the surgeon should avoid clamping of the aorta to avoid atherosclerotic microembolization of renal artery branches. Other authors suggest that surgical embolectomy be reserved for patients with total parenchymal embolization whose condition has failed to respond to less invasive models of therapy²³. The largest series of the surgical management of RATE reported an operative mortality of 5.5%. Almost half of the patients were normotensive after surgery and 89% had a radiographically patent renal artery²⁴. Similar results have been published for smaller series^{25,26}.

Thrombolytic techniques have also been shown to produce promising results, although there have been no prospective randomized studies comparing different treatment modalities²⁷⁻³⁰. Medical therapy will improve renal function only if there is incomplete occlusion or if effective thrombolysis is initiated within 90 to 180 minutes. Unfortunately, the diagnosis of renal embolization is often delayed. Since fibrinolytic therapy was successfully introduced by Halpern *et al.*¹⁶, a lot of reports have been pub-

lished on the use of percutaneous transfemoral approach and local infusion of streptokinase, urokinase or tissue plasminogen activator, with or without balloon angioplasty, especially when the embolism takes place at intra-renal arteries^{31,32}. Urokinase is currently given immediately after arteriography, *via* a catheter in the main renal artery at the initial dose of 4,000 IU/min for 2-4 hours, then at a reduced dose of 1,000-2,000 IU/min for 8 hours or longer. Radiological control is used to monitor the embolus. If it persists, urokinase perfusion is prolonged; if revascularization is achieved, the catheter is removed and sodium heparin perfusion is administered for 24 hours to keep the activated partial thromboplastin time ratio at 1.5-2. A long time lapse after embolism should not be considered a contraindication for revascularization when arteriography shows signs of viability. In those patients in whom either surgery or fibrinolytics are contraindicated, treatment with heparin should be considered in order to avoid further embolic episodes. In those who are actively bleeding or with critical clinical status only conservative measures are indicated. Although encouraging results have been reported with intra-arterial fibrinolytics, complications may include uncontrolled bleeding, pseudoaneurysms, distal embolization, acute mesenteric embolism, pericatheter thrombosis, allergic reactions, and strokes³³. Success rates of 70%-86% are reported³⁴. The exclusion criteria for fibrinolytic therapy have been generally accepted and are based on the Consensus Development Conference Statement of the US National Institutes of Health³⁵.

Transcatheter clot aspiration is a very successful technique. After clot aspiration, the kidney should be perfused with a fibrinolytic agent (tissue plasminogen activator). Continual heparinization and later warfarinization should follow. Anticoagulation should be lifelong after thromboembolism, unless a contraindication exists.

Percutaneous rheolytic therapy with the angiojet atherectomy catheter is a successful novel method for RATE treatment³⁶. Although transcatheter clot aspiration and percutaneous rheolytic therapy are a less invasive option than surgery and thrombolysis in the severely ill patients with cardiovascular disorder, their use still carries a certain risk.

Antihypertensive therapy may be required after RATE. An elevation in blood pressure may develop during the first week, and usually but not always begins to subside within 2 to 3 weeks. The increased renin release tends to play an important role, and therapy with ACEi is effective.

Success of RATE Treatment

Success in the management of RATE lies in the early diagnosis and prompt appropriate treatment. The duration of renal ischemia is important, but it does not correlate directly with renal damage, especially if incomplete obstruction or collateral circulation is present. Recovery of renal function in humans was believed to be successful when revascularization occurred before 90 min to 18 h of the onset of symptoms³⁷. In the literature, there are cases of spontaneous recovery or successful late embolectomies at 43 days from the onset of symptoms. Despite successful revascularization, the parameters of renal function can almost never reach those prior to RATE and kidney shrinkage becomes a frequent consequence^{33,38}. With better control of cardiac arrhythmias and use of anticoagulants in patients with atrial fibrillation, the incidence of RATE will probably be lower.

Despite the efficacy of medical treatment, the early and late mortality from clot emboli remains high due to both extrarenal embolization (particularly to the brain and intestine) and underlying disease (atherosclerotic heart disease).

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Sažetak

Tromboembolija bubrežne arterije: neprepoznati uzrok akutnog bubrežnog zatajenja

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Akutna tromboembolija bubrežne arterije je kritično stanje za bolesnika. Značajan je, ali često pogrešno dijagnosticiran te potencijalno reverzibilan uzrok ishemijske bolesti bubrega. Ova se bolest često previda, a rana i ispravna dijagnoza vode ka ispravnom liječenju uz dobre izgleda za oporavak bubrežne funkcije i izbjegavanje nepotrebnih, agresivnih dijagnostičkih i terapijskih postupaka. Kada se susretnemo s bolesnikom koji ima akutno bubrežno zatajenje i atipičnu bol u križima ili trbuhu, poglavito u onih s visokim čimbenicima rizika, preporučamo provođenje dijagnostičkog postupka koji se temelji na određivanju serumske razine laktat dehidrogenaze u kombinaciji s ostalim dijagnostičkim metodama i postupnikom za liječenje tromboembolije bubrežne arterije.

Ključne riječi: