Renal cell carcinoma (RCC) represents 3% of adult malignancies, and it affects approximately five to 13 patients per 100,000 individuals in Western countries. RCC has the propensity to enlarge rapidly and disseminate locally, which frequently results in a highly vascular tumor with local structural invasion. As a result, patients with RCC often present with gross hematuria, flank pain, and palpable abdominal mass. Studies have demonstrated that up to 20% of patients with primary RCC have some degree of tumor thrombus extending into the renal pelvis, inferior vena cava, and even the hepatic veins. Although nephrectomy is the only curative form of therapy, as well as the treatment of choice of primary RCC, surgical treatment can present a daunting challenge due to intraoperative hemorrhage associated with excision of these highly vascularized and locally invasive tumors.

In an effort to improve the surgical management of RCC, physicians began to intentionally induce necrosis of the cancerous kidney by transarterial injection of thrombotic agents. Almgard et al first proposed transarterial renal embolization as a means to induce kidney necrosis in 1973. Since then, it has become an accepted form of treatment in advanced or unresectable renal cell tumors with persistent bleeding or manifestations of paraneoplastic syndrome. Moreover, it has evolved to become an accepted preoperative adjunct to nephrectomy.

Although the predominant benefit of preoperative renal embolization is the reduction of operative blood loss associated with nephrectomy, many have noted that it also decreases vena caval tumor size and creates an easier dissection plane as a result of tissue edema. Transarterial embolization of RCC has also been utilized to palliate patients with nonresectable tumors and severe symptoms such as hemorrhage or flank pain.

Transarterial renal embolization of RCC is typically...
performed percutaneously several days prior to the removal of the carcinomatous kidney. Because of renal infarction as a result of the embolization, patients often experience severe flank pain and fever after the procedure, leading to a condition also known as the postinfarction syndrome. In addition, the staged treatment strategies often created added emotional anxiety to patients and families due in part to the time delay between transarterial renal embolization and nephrectomy. This article discusses the indication, techniques, and pitfalls of transarterial renal embolization of RCC. In addition, we analyzed our experience and outcome of intraoperative renal artery embolization with concomitant nephrectomy in the treatment of RCC.

**INDICATIONS FOR TRANSARTERIAL RENAL EMBOLIZATION**

The two main indications for renal artery embolization in RCC are to (1) facilitate operative resection of a hypervascular carcinomatous kidney, and (2) provide palliative treatment in patients with symptomatic or inoperable RCC.

Several factors should be considered when planning renal artery embolization as an adjunctive measure prior to the nephrectomy. Preoperative embolization is beneficial in cases of large hypervascular kidney because it can reduce intense bleeding during surgery. The goal is to facilitate surgical nephrectomy by reducing operative time as well as blood loss. When the carcinomatous kidney is large and hypervascular, enlarged tortuous renal veins usually cover the surface of the neoplasm and the renal hilum. Frequently, regional lymph node metastases or tumor thrombus in the inferior vena cava or renal vein may impede access to the renal artery during the nephrectomy procedure. Preoperative renal artery embolization invariably leads to the collapse of these large venous tributaries, which would facilitate both nephrectomy and tumor thrombectomy. Moreover, the infarcted kidney typically becomes edematous, which creates a more definable surgical plane surrounding the carcinomatous kidney. Various embolic materials have been utilized for this purpose (Table 1).

Palliative renal artery embolotherapy may be considered in patients with advanced or unresectable renal tumor. Alternatively, renal artery embolization may provide a palliative means in symptomatic patients who are inoperable due to poor general health conditions. The ideal thrombotic agent of palliative renal artery embolotherapy remains a matter of debate, with many choices listed in Table 1. Many of these embolic materials have been studied extensively only to yield disappointing long-term outcomes. For the purpose of therapeutic palliative embolotherapy, it is logical to choose an embolic agent that not only can achieve total tumor necrosis by means of capillary embolization but can also cause thrombotic occlusion of parasitic collateral vessels. One such embolic agent that can result in complete renal tumor ablation is ethanol. Catheter-directed transarterial chemoembolization associated with selective renal artery embolization of RCC has been evaluated in limited clinical studies recently, and outcome remains elusive at the present time.

**TECHNIQUES AND EMBOLIC AGENTS OF RENAL ARTERY EMBOLIZATIONS**

The efficacy of different types of embolic agents has been analyzed extensively, both in clinical and animal studies. In studies conducted during the 1980s, autolo-
gous muscle particles, gelatin foam, or metal coils were commonly used. Short-acting embolic agents, such as thrombin or absorbable gelatin sponge could adequately achieve preoperative devascularization of cancerous kidney. However, permanent materials, such as alcohol or metal coils, were preferred if the objective was to induce permanent thrombosis or long-term palliation.

“Absolute ethanol has become the preferred embolic agent in recent years for all transarterial renal embolization.”

Absolute ethanol has become the preferred embolic agent in recent years for all transarterial renal embolization. Ethanol is inexpensive, easy to obtain, readily available in sterile form, and can be injected easily through standard interventional catheters. When injected into the renal artery, concentrated ethanol denatures protein rapidly and causes perivascular necrosis within the renal parenchyma. It also causes erythrocyte sludging and microvascular occlusion, which leads to endothelium sloughing into the lumen, resulting in ischemic necrosis. Ethanol has an advantage over other embolic agents because arterial recanalization is avoided and collateralized vessels are unlikely to form, which minimize the risk of secondary hypertension. However, severe complications related to alcohol injection can occur, which will be described subsequently in this article.

Regarding the technical steps of renal artery embolization, the patient is first positioned in the supine position on an angiosuite table. If this is performed as a preoperative adjunctive procedure several days prior to the nephrectomy, it can be performed under local anesthesia with minimal intravenous sedation if necessary. On the other hand, if renal artery embolization is performed concomitantly during a nephrectomy operation, general anesthesia via orotracheal intubation should be established so the combined procedures can be performed. The contralateral femoral artery (opposite to the RCC) was accessed percutaneously followed by the placement of a 6-F introducer sheath (Boston Scientific Corporation, Natick, MA). After the placement of a standard pigtail catheter (Boston Scientific) over a .035-inch Bentson guidewire (Boston Scientific), an aortogram is performed to identify the renal artery feeding the RCC. A renal double curve catheter (RDC, Boston Scientific) is placed over a .035-inch Bentson guidewire to cannulate the renal artery. If detachable coils are used to induce renal artery occlusion, a 7-F multipurpose guiding catheter (Boston Scientific) is placed over the Bentson guidewire and positioned in the proximal renal artery. The RDC catheter is inserted into the renal artery through the guiding catheter whereby detachable coils ranging in size from 3 mm to 7 mm are inserted in the distal portion of the main renal artery. If concentrated alcohol is the embolic agent, it can be mixed with iodized oil to increase its radiopacity and infused directly via a selective renal artery catheter. Completion renal angiography is performed to demonstrate total occlusion of the renal artery by the embolic agents.

**COMPLICATIONS OF RENAL ARTERY EMBOLIZATION**

There are many reports of procedural-related complications associated with renal artery embolization in the management of RCC. One of the most frequent complications is unintentional embolization of peripheral arteries of the lower extremities due to reflux or dislodgment of embolus, which can occur in as many as 10% of cases. This complication may require emergent operative embolectomy via a femoral artery cutdown. Other devastating complications due to inadvertent embolization of other organs have been reported, with resultant bowel infarction and spinal cord infarction. In a study that evaluated preoperative renal artery embolization, complications related to inadvertent occlusion of nontarget vessels is 4.9%, with a overall mortality rate of 1.2%. Given the serious morbidity related to inadvertent embolization, great care must be taken during the injection of embolizing agents to minimize this complication. The injection catheter should be placed well within the target renal artery rather than near the renal artery ostium.

Another common complication is postinfarction syndrome, which occurs 1 to 3 days after renal artery embolization. This syndrome consists of fever, flank pain, nausea, and vomiting. The formation of gas released from the infarcted kidney due to necrosis as seen on CT scans or ultrasound examination after renal artery embolization has been characterized as a part of the syndrome. The introduction of ethanol as an embolic agent to replace gelatin foam in the early 1980s was associated with a reduction in the incidence as well as in symptoms of postinfarction syndrome. Lammer et al reported a complication rate of 9.9% in 121 renal tumor embolizations with a mortality of 3.3%. Due in part to the large carcinomatous kidney mass and the severely impaired medical conditions of these
patients, the complication rate in palliative embolizations was approximately four times as high as in preoperative procedures.\textsuperscript{14}

Several researchers have compared the complication rate of various embolic agents. In a study reported by Lammer et al, the complication rate was higher with polyvinyl alcohol than with gelatin foam.\textsuperscript{14} However, ethanol resulted in a significantly decreased frequency of nausea and vomiting after embolization compared with gelatin foam.\textsuperscript{22} Other studies also found that ethanol has the lowest complication rate, a milder postinfarction syndrome, and causes a greater degree of occlusion in shorter time.\textsuperscript{23,24}

Hypertension is another potential complication, particularly when there is incomplete infarction of the kidney. It is likely caused by the increased renin production of the ischemic renal parenchyma.\textsuperscript{25} Therefore, it is important to document a complete occlusion of the arterial inflow to the target kidney, as confirmed by postembolization arteriograms. Recurrent renal artery canalization may occur, but the embolic agents currently used today are quite effective in achieving complete renal occlusion with a low likelihood for this possibility. Renal failure can occur after renal artery embolization, but is likely related to the use of large volumes of contrast material during the procedure.\textsuperscript{25}

To avoid this complication, care must be taken to limit the amount of contrast agents, and the patient should be well-hydrated before and after the embolization procedure. Lastly, infection is another potential complication, although the incidence of this problem remains low. Two risk factors have been identified that may be associated with an increased risk of infection—patients with immunocompromised illness and renal calculi. Patients who are considered to undergo renal artery embolization should be stone-free and have no overt evidence of urinary tract infection before the procedure. Broad-spectrum antibiotics should be given intravenously immediately before and after the embolization procedure.

**Techniques to Reduce Procedure-Related Complications**

To reduce the incidence of inadvertent embolization of a nontarget vessel due to aortic reflux, many researchers have discovered the utility of delivering the embolic agent via a balloon catheter.\textsuperscript{26} In this scenario, a balloon catheter is placed in the renal artery over a guidewire. After the inflation of the balloon catheter, which occludes the renal artery inflow, the embolic agent is delivered through the guidewire lumen. This maneuver reduces the arterial reflux due to aortic flow, which can minimize the possibility of inadvertent embolization of nontarget vessels.

Other researchers have described various techniques of enhancing the radiopacity of alcohol when administered as an embolic agent.\textsuperscript{27,28} De Baere et al used ethanol emulsified with an iodized oil mixture, which provided high radiopacity and allowed good control of the mixtures when injected in the renal artery.\textsuperscript{26} Others have reported mixing ethanol with nonionic contrast medium, but precipitation occurred and was believed to be the cause of death in one patient.\textsuperscript{27,28} In addition, contrast medium induces ethanol dilution, which decreases its thrombotic efficacy. The effect of contrast medium dilution does not occur with iodized oil when emulsified with ethanol. Iodized oil acts as a plastic embolus that travels through the arterial circulation and prolongs the dwell time between ethanol and the vascular endothelium, which overall increases the thrombotic efficacy in this mixture.\textsuperscript{30}

Although ethanol injection alone is sufficient in inducing arterial thrombosis, many researchers have reported that combining ethanol-induced sclerosis in parenchymal branches with proximal absorbable gelatin sponge and coil plugging proved beneficial for immediate and permanent interruption of renal arterial flow. This combination prevents revascularization of the proximal renal artery via short branch collaterals, such as the diaphragmatic or ureteral arteries, which may not be initially embolized with ethanol injection. A possible mode of failure with ethanol renal embolization can be caused by such insufficient ostial ablation.

With regard to the management of postinfarction syndrome, patients may experience flank pain after renal artery embolization and the pain severity seems to be directly related to the extent of embolized renal tissue.\textsuperscript{25} Pain symptoms related to the postinfarction syndrome can be managed with intra-arterial renal injection of 1 mL of bupivacaine just before ablation or 2 mL lidocaine.\textsuperscript{31} Some researchers advocate the use of epidural anesthesia as a standard protocol for renal artery embolization, which can be used for several days if necessary to ensure adequate pain control prior to the nephrectomy procedure.\textsuperscript{26}
A clinical study was conducted at our institution during a recent 6-year period ending in November 2004 in which patients with complex RCC underwent combined intraoperative renal artery embolization and nephrectomy (Figure 1). A total of 12 patients (mean age, 63 ± 9 years) were identified. Preoperative CT scan of the abdomen demonstrated evidence of tumor extension into the inferior vena cava in four patients (33%) and retrohepatic vein in three patients (25%). For the purpose of comparison, these patients (combined treatment group) were compared to a cohort group of 14 patients (staged treatment group) with primary RCC who underwent staged renal artery embolization and nephrectomy during the same study period. Data regarding patient demographics, intraoperative parameters, and clinical outcome were analyzed between the two groups and are summarized in Table 2. Hospital cost data, rather than hospital charges, were assessed by directly obtaining the pertinent information from the hospital accounting department. Hospital costs per each expenditure category between the two groups of patients were also compared. Statistical analysis was performed by means of the Student t test and the Fisher exact tests. The test results were considered significant at a P value <.05.

For the purpose of cost analysis, four expenditure categories encompassing all inpatient hospital costs were defined as: (1) operating room cost, which included operating room time, anesthesia time, equipment cost, operating room nursing, and recovery room costs; (2) room cost, which included regular floor, telemetry bed, and intensive care unit cost; (3) radiology cost, which included all diagnostic or therapeutic procedures, such as renal artery embolization, plus plane radiography, ultrasound scan or other diagnostic imaging; and (4) other costs, which included pharmacy, transfusion, and laboratory services.

STUDY OUTCOME

Outcome of group comparison in this study has been previously reported. The renal cell tumor was successfully resected in all patients. Renal artery embolization was also successfully performed in both the combined and staged treatment groups. When comparing the clinical variables between the two groups, an increased length of hospital stay was noted in the staged treatment group when compared to the combined treat-
ment group (5.6 ± 1.3 days vs 10.2 ± 3.2 days; \( P = .02 \); Table 2). No patients in the combined treatment group had postinfarction syndrome. However, such a syndrome occurred in four patients who underwent the staged treatment (\( P = .03 \); Table 2). Although the operative time in the combined treatment group was greater than the staged treatment group, the difference did not reach a statistical significance (Table 2). Intraoperative autologous red blood cell transfusion (2 units) was necessary in only one patient (13%) in the combined treatment group. There was no perioperative mortality in either group in our series. The mean volumes of contrast medium used in the combined treatment and staged treatment groups were 20 mL and 25 mL, respectively (\( P = .85 \)). Two patients (25%) in the combined treatment group underwent caval reconstruction using interposition polytetrafluoroethylene grafts, which was performed by a vascular surgeon after the caval tumor thrombectomy. In contrast, concomitant caval reconstruction was necessary in four patients (29%) in the staged treatment group. No patient in the combined treatment group developed postoperative renal dysfunction, which was defined by elevation of serum creatinine greater than 15% of the baseline level. In contrast, one patient (7%) in the staged treatment group developed postoperative renal insufficiency. During the follow-up period, three patients died due to myocardial infarction, one patient died 3 years later because of osteomyelitis, and two patients died of Alzheimer’s disease. There was no evidence of tumor recurrence in the surviving patients in either group.

Comparison of the hospital cost in four expenditure categories revealed significantly increased room cost ($4,652 ± $1,025 vs $9,832 ± $1,952; \( P < .01 \)) and radiology cost ($952 ± $452 vs $3,250 ± $85; \( P < .02 \)) in the staged treatment group when compared to the combined treatment group. Although the combined treatment group had slightly higher operating room costs ($3,652 ± $1,525 vs $3,158 ± $927; \( P = .23 \)) and less cost in the other expenditure category ($865 ± $336 vs $1,235 ± $419; \( P = .08 \)), these costs were not significantly different when compared to the staged treatment group. Lastly, the mean total hospital cost was significantly lower for patients who underwent the combined treatment compared to the staged treatment group (mean cost difference was $9,214; \( P = .02 \)).

**POTENTIAL BENEFITS OF A COMBINED RENAL EMBOLIZATION WITH CONCOMITANT NEPHRECTOMY**

There are several advantages to this combined treatment strategy when compared to the traditional staged treatment approach. First of all, the renal artery embolization and nephrectomy are coordinated in a single stage so the patient would receive one general anesthesia while undergoing two planned procedures. This strategy provides a benefit of minimizing the undue emotional strain and mental anxiety associated with two procedures performed separately in the radiology suite and operating room. We previously described our experience of concomitant inferior vena cava filter placement in patients undergoing major orthopedic procedures, and noted that patients experienced less anxiety when two procedures are performed jointly under the same general anesthesia rather than performed separately in the radiology suite and operating room. Second, because the nephrectomy is performed immediately after the renal embolization, it avoids the possibility of postinfarction syndrome. In this scenario, patients are not subjected to the physical pain or emotional distress associated with tumor infarction. Studies have shown that abscess formation or sepsis may occur after tumor embolization prior to nephrectomy, particularly in patients with indwelling nephrostomy tubes due to obstructing RCC. Weckermann et al have also shown that if nephrectomy is performed more than 4 days after renal artery embolization, emphysematous pyelonephritis may occur as evidenced by intrarenal gas formation on the abdominal CT scan. In this circumstance, the mortality rate due to septic complications of postinfarction syndrome can reach as high as 10%. Our study demonstrated the benefit of the combined treatment in which no patient experienced postinfarction syndrome. In contrast, postinfarction syndrome occurred in 36% of patients who underwent the staged treatment. Another advantage of the combined treatment relates to the reduced hospital cost. The cost analysis of this study showed a significant reduction in the hospital room cost and radiology cost in those who underwent the combined treatment when compared to the staged treatment group. The reduction in the room cost was largely related to the decreased hospital length of stay in the combined treatment group, because those who received the staged treatment waited an average of 3.3 days after renal embolization before undergoing nephrectomy.

Despite these potential advantages, it is noteworthy that one potential disadvantage of this combined approach may exist, which is related to renal dysfunction associated with contrast administration and nephrectomy. Although no patients in our series developed renal failure after concomitant renal artery embolization and nephrectomy, we postulate such a complication is possible if excessive contrast medium is given in a dehydrated...
patient undergoing nephrectomy. In our series, vigilant efforts were made to limit the amount of contrast medium used in renal artery embolization. Furthermore, a central venous catheter was used peroperatively in all patients to ensure they were well hydrated to minimize the likelihood of renal dysfunction.

CONCLUSIONS

Renal artery embolization has been proven to be a useful adjunct in the surgical management of large hypervascular RCC. Interventionists who perform this procedure must be cognizant of the technical pitfalls and complications related to this procedure. Our study illustrates the role of this adjunctive endovascular procedure that facilitates a conventional open operation. Intraoperative renal embolization can minimize blood loss and facilitate nephrectomy when performed jointly as a combined procedure. Moreover, we believe this approach minimizes postinfarction syndrome and reduces hospital cost when compared with the traditional staged treatment approach. Additional clinical studies will be necessary to further validate the benefit of this combined treatment strategy in patients with RCC.

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