Correspondence

Cryoplasty for the Treatment of In-Stent Renal Artery Stenosis?

To the Editor:

We read with interest the case report by Jefferies and colleagues[1]—"First Use of Cryoplasty to Treat In-Stent Renal Artery Stenosis"—concerning a patient whom they treated in April 2005. We would like to share our own experience on the subject, which antedates the authors' experience by 1 calendar year.

We used cryoplasty to treat 2 patients who presented at our institution with renal in-stent restenosis in March and April 2004. The 1st patient had undergone treatment of in-stent stenosis of the right renal artery by conventional percutaneous transluminal angioplasty (PTA) 3 times in the preceding 26 months. The patient presented with worsening hypertension and a critical, near-occlusive (99%) in-stent stenosis, which was treated with PTA to 6 mm and then with cryoplasty, by use of a 6-mm PolarCath™ (CryoVascular Systems, part of Boston Scientific Corporation; Natick, Mass). The treatment resulted in a residual stenosis of less than 30%. Intra-arterial pressure measurements, which were performed before and after the procedure, showed a decrease of the systolic peak-to-peak gradient from 138 mmHg to 3 mmHg. The patient was discharged from the hospital the next day. Six months after the intervention, a computed tomographic angiogram revealed a recurrent stenosis of 60% to 70%. The patient was finally referred to vascular surgery for a renal artery bypass to correct the refractory in-stent stenosis.

The 2nd patient had received adjuvant radiation treatment for acinar cell carcinoma of the pancreas and had developed left renal artery stenosis due to radiation arteritis. The stenosis was treated with a stent in 1998. Worsening hypertension and Doppler sonographic evidence of significant in-stent restenosis led to retreatment with conventional PTA in April 2000, March 2001, and August 2002. In April 2004, the patient presented again, with recurrent hypertension and worsening renal insufficiency. Angiography performed with carbon dioxide showed a stenosis of 70% to 80%, which was treated first with PTA to 6 mm and then with cryoplasty to 5 mm. Follow-up angiography showed a widely patent stent, and the patient was discharged from the hospital the next day. In January 2006, Doppler ultrasonography showed left renal artery occlusion due to in-stent thrombosis, which was confirmed angiographically. Angioplasty performed to 4 mm was followed by the placement of a 5- × 16-mm iCAST™ covered stent (Atrium Medical Corporation; Hudson, NH), which was post-dilated to 6 mm. Control angiography showed an excellent result, with a widely patent left renal artery. Six months later, the patient presented with acute onset of left-flank pain, and with elevated creatinine levels upon hospital admission. Angiography performed that day showed near-occlusion of the stent, which was successfully crossed and treated first with PTA to 4 mm and then with cutting-balloon angioplasty (5-mm system). This procedure was complicated by a non-flow-limiting dissection in the renal artery distal to the stent and by a filling defect in the stent, which was thought to be a thrombus. Catheter-directed thrombolysis with Activase® r-TPA (Genentech, Inc.; South San Francisco, Calif) was performed for 4 hours and resulted in considerable improvement. However, a substantial amount of material (thought to be intimal hyperplastic tissue) remained in the stent, and the patient subsequently underwent aorto-renal bypass with the use of a reversed autologous saphenous vein. This surgery was itself complicated by a stenosis in the graft, which was successfully treated by means of PTA.

By providing the radial force to offset the elastic recoil of PTA-resistant lesions, stenting has revolutionized the treatment of renal artery stenosis. However, stenting can lead to epithelial in-growth, and the treatment of resultant hemodynamically significant in-stent stenoses remains problematic. Different procedures are being or have been used for the treatment of in-stent stenosis—including repeat PTA, the use of cutting balloons, restenting with bare-metal and uncovered stents, endovascular brachytherapy, laser-assisted procedures, atherectomy, drug-eluting stents, and cryoplasty—but few hard data are available to show the clinical efficacy of most of these. Zeller and colleagues[2] reported on a prospective series of 31 patients who had 33 in-stent stenoses of the renal arteries and who had undergone prior treatment for the same. The investigators saw a benefit to restenting in comparison with conventional PTA, but the difference was not statistically significant. Of note, the authors did report a statistically higher rate of restenosis with the use of a cutting balloon. The overall restenosis in their series was 36% over a 12-month interval; PTA alone was associated with a recurrence rate of 71%, versus 43% for bare-metal stenting and 17% for covered stenting. The use of a cutting balloon resulted in 100% restenosis in the 3 patients thus treated. Restenosis was more likely to occur in renal arteries of smaller diameters. Of 4 patients who received drug-eluting stents, none developed restenosis. N'Dandu and associates[3] reported similar results in their series of 34 patients who had 41 in-stent restenoses. Compared with

the PTA group, the stent group experienced a better reduction of stenosis after the procedure, better secondary patency, and increased freedom from recurrent in-stent stenosis. However, the restenosis rate in this series was still 29% for the stent group.

Brachytherapy has been used by several investigators with some success.[4,5] The investigators in the largest published series to date[5] used gamma-radiation brachytherapy and reported a 12-month restenosis rate of 20% in 10 patients thus treated who survived 1 year. The use of cutting-balloon angioplasty for renal in-stent stenosis has been described in a case report[6] (as in the Jefferies report and that of our patients), but it is doubtful that the use of this method can improve freedom from restenosis.

Drug-eluting stents might prove advantageous; however, except in isolated reports,[2,7] clinical proof of the superiority of drug-eluting stents over PTA or bare-metal stent is currently lacking. In addition, the only prospective study on the subject, the GREAT trial,[8] showed no statistically significant advantage of drug-eluting stents over bare-metal stents in the treatment of native renal artery stenoses.

The PolarCath™ Peripheral Dilatation System (Boston Scientific) is indicated for the dilation of stenoses in the peripheral vasculature, including the iliac, femoral, popliteal, infrapopliteal, renal, and subclavian arteries. Almost all of the available relevant literature examines the use of the device in the lower-extremity arterial system. Interestingly, cryoplasty has yet to show benefit over angioplasty alone as a primary treatment, even in the femoropopliteal arteries.[9]

No large series or randomized-control trial has been published about cryoplasty in the treatment of renal artery in-stent stenoses. Karthik and co-authors[10] reported no benefit from cryoplasty versus PTA in the treatment of restenosis in the iliofemoral segments. Samson and colleagues[11] reported on 2 patients who were treated with cryoplasty for in-stent stenosis—one in a femoral artery stent, the other in a popliteal artery stent—and both patients experienced restenosis, one at 4 months and one at 12 months.

The reports in the medical literature and our own experience have led us to conclude that cryotherapy does not offer any benefit over balloon angioplasty alone in the treatment of in-stent stenosis. In fact, the added cost of $1,700 per procedure compared with PTA alone has caused others (and us) to abandon cryoplasty as a therapeutic option altogether.[11]

Last, we would like to comment on the Doppler sonographic follow-up of the patient who was described by Jefferies and co-authors. Although clinical evidence of restenosis might not have been apparent, an ultrasonographic peak of 21 mmHg is abnormal and generally indicates a stenosis in the 50% range. An arterial gradient of 20 mmHg is considered the cutoff as an indication for intervention, according to the Society of Interventional Radiology FDA Device Forum Committee and to the American Heart Association's councils on Cardiovascular Radiology, High Blood Pressure Research, Kidney in Cardiovascular Disease, Cardio-Thoracic and Vascular Surgery, and Clinical Cardiology.[12] We believe that most interventional practitioners would treat a lesion that has such a gradient.

In summary, we believe that the efforts of Dr. Jefferies and his colleagues to treat the in-stent stenosis in their patient are commendable. However, their conclusion that cryoplasty can be safely and effectively performed in the renal arteries for treatment of in-stent stenosis is supported neither by their case nor by our 2 cases.

The successful treatment of renal in-stent stenosis remains a clinical challenge, and all current data suggest that it cannot be adequately treated with cryoplasty.

Daniel E. Hendricks, MD,
Klaus D. Hagspiel, MD,
University of Virginia Health System,
Charlottesville, Virginia

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This letter was referred to Dr. Zvonimir Krajcer, who replies in this manner:

I agree with the authors' comments, which are on the basis of their 2 cases, that there is no ideal solution to in-stent restenosis after renal artery stenting. Many options and methods exist, but none has proved to resolve this condition in all patients. The case of our patient reveals that our approach was correct in resolving this complex problem of renal artery in-stent stenosis. The evidence of this is that our patient has continued to do well since the procedure.

Zvonimir Krajcer, MD,
Department of Cardiology,
Texas Heart Institute
at St. Luke's Episcopal Hospital,
Houston, Texas