Right-Side Colon Ischemia: Clinical Features, Large Visceral Artery Occlusion, and Long-Term Follow-Up

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ABSTRACT

Context: Large visceral artery occlusion (LVAO) could underlie right-side colon ischemia (RSCI) but is little known.

Objective: To assess patients with RSCI through long-term follow-up, including features and management of LVAO.

Main Outcome Measures: Mesenteric ischemia and mortality.

Design: Retrospective observational study in an integrated health care system.

Results: Of 49 patients (30 women [61.2%]; mean [standard deviation] age, 69.4 [11.9] years), 19 (38.8%) underwent surgery—that is, 5 (83.3%) of 6 who developed RSCI in hospital following surgical procedures and 14 (32.6%) of 43 who had RSCI before hospitalization (p value = 0.03); overall, 5 (10.2%) died. Among 44 survivors with a median (range) follow-up of 5.19 (0.03-14.26) years, 5 (11.4%), including 3 (20.0%) of 15 operated cases, had symptomatic LVAO and underwent angioplasty and stent placement: 2 for abdominal angina that preceded RSCI, 1 for acute mesenteric ischemia 1 week after resection of RSCI, 1 for RSCI 6 weeks after resection of left-side ischemia, and 1 for abdominal angina that began 3 years after spontaneous recovery from RSCI. None had further mesenteric ischemia until death from nonintestinal disease or the end of follow-up (1.6 to 10.2 years later). Kaplan-Meier survival estimates for all 44 survivors at 1, 3, 5, and 10 years were 88.6%, 72.3%, 57.6%, and 25.9%, respectively. Thirty-one patients (70.4%) died during follow-up, 19 (61.3%) of a known cause; the 39 patients not treated for LVAO lacked mesenteric ischemia.

Conclusion: Patients with RSCI may have symptomatic LVAO; therefore, we advise they undergo careful query for symptoms of abdominal angina and routine visceral artery imaging.

INTRODUCTION

Colon ischemia (ischemic colitis) varies in extent from mucosal and submucosal ischemia to transmural infarction and in severity from reversible to fatal disease.[1,2] In left-side colon ischemia, the most common type, the ischemic segments typically correspond to the "watershed" areas of potentially limited collateral flow between the superior mesenteric artery (SMA) and inferior mesenteric artery (IMA) circulations or between the superior hemorrhoidal artery and IMA circulations, affecting the descending colon and sigmoid colon, respectively. Vascular imaging is rarely helpful. In contrast, rates of surgery and mortality are much greater after right-side colon ischemia (RSCI),[3-7] suggesting a different pathophysiology in some cases, including large artery disease. A committee comprised of three gastroenterologists and one surgeon that recently developed practice guidelines for colon ischemia cited anecdotal evidence that RSCI can herald acute mesenteric ischemia caused by large artery occlusion. Therefore, they advised routine computed tomographic (CT) angiography for patients with RSCI, but they found no published supporting data.[1] There is also little information on other aspects of the long-term outcome of survivors of RSCI, including recurrent mesenteric ischemia, other morbidities, and rates of death and its causes.

The importance of diagnosing and treating large visceral artery disease is emphasized by the severe nature of acute mesenteric ischemia[8,9] and the effectiveness of therapy.[10] We assessed the clinical characteristics and treatment of patients hospitalized for RSCI and their long-term outcome, including the features of large visceral artery occlusion diagnosed from the index episode of RSCI until follow-up ended, as well as morbidity and mortality during follow-up.

MATERIALS AND METHODS

The patients were members of Kaiser Foundation Hospitals and Health Plan in San Diego, CA, a prepaid, integrated health care system serving more than 500,000 people. Most patients were treated at the Kaiser Permanente (KP) hospital, and the records included reports on cases treated at a contract hospital or other facility. The studied cases were included in a report of 417 consecutive episodes of acute colon ischemia of various large bowel segments in 401 patients: left side, 363 (87.1%); right side, 39 (9.4%); bilateral (extension of ischemia distally to at least the splenic flexure), 10 (2.4%); and transverse only, 5 (1.2%). Because there is no unique International Classification of Diseases, Ninth Clinical Modification (ICD-9-CM) code for colon ischemia, the primary author reviewed inpatient records of all patients with ICD-9-CM

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code 557.0 (acute vascular insufficiency of intestine), 557.1 (chronic vascular insufficiency of intestine), or 557.9 (unspecified vascular insufficiency of intestine) from January 1, 2000, through December 31, 2006. Patients without colon ischemia or with mechanical obstruction, pseudo-obstruction, or small bowel ischemia were excluded and assigned levels of diagnostic evidence according to clinical and testing criteria. Epidemiologic and other data from patients with ischemia of any part of the large bowel were combined for most analyses.[11]

In the present study conducted in 2014 on the 49 patients who had 1 episode of RSCI (including 10 with bilateral ischemia), the primary author reviewed prehospitalization outpatient records and posthospitalization outpatient and inpatient records and entered data into a spreadsheet application (Excel v14; Microsoft, Redmond, WA). The final follow-up date was the date of records review for current KP members, disenrollment from KP, or death, using the earlier of the latter 2 dates. Disenrollment dates were recorded in an institutional electronic database, and death dates were obtained from KP records, the State of California Department of Health and Human Services, and the Social Security Administration (available through 2012 from the latter 2 sources). For patients who had died while KP members, causes of mortality were determined from medical records, including death certificates. The KP institutional review board approved the study.

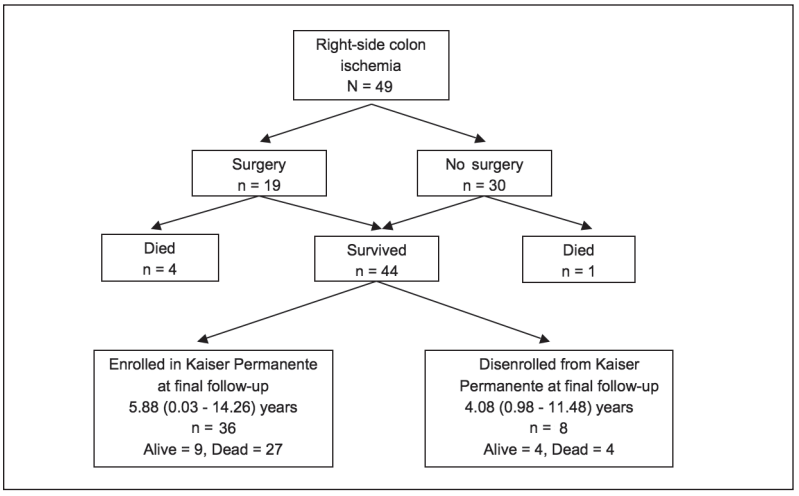

Figure 1. Treatment and outcome of patients, including Kaiser Foundation Hospitals and Health Plan enrollment status at final follow-up, with follow-up duration summarized as median (range).

Table 1. Chronic comorbidities in 49 patients with right-side colon ischemia[a]

Disease	No. (%)
Hypertension	36 (73.5)
Hyperlipidemia (drug-treated)	18 (36.7)
Coronary artery disease	13 (26.5)
Diabetes	13 (26.5)
Atrial fibrillation	9 (18.4)
Congestive heart failure	8 (16.3)
Cerebrovascular disease	7 (14.3)
Depression (drug-treated)	7 (14.3)
Peripheral vascular disease	7 (14.3)
Chronic renal disease (dialysis-dependent)	5 (10.2)
Chronic obstructive pulmonary disease	5 (10.2)
Dementia	3 (6.1)
Miscellaneous[b]	11 (22.4)

[a] The total exceeds 49 because of patients with multiple comorbidities.
[b] Valvular heart disease in 2 patients (4.1%); 1 patient (2.0%) each with celiac disease, cocaine ingestion, chronic myelogenous leukemia, metastatic prostate cancer, myelodysplasia, pulmonary sarcoidosis, progressive systemic sclerosis lung disease, sleep apnea, or thrombotic thrombocytopenic purpura.

We summarized normally distributed continuous data as mean (standard deviation [SD]) and data not normally distributed as median (range). Statistical analysis comprised the Wilcoxon 2-sample test for continuous variables and Fisher exact test for categorical variables, accepting statistical significance as 0.05 by 2-tailed testing. Survival after discharge was analyzed using the Kaplan-Meier method.

RESULTS

The 49 patients who had RSCI ischemia included 30 women (61.2%) who were 69.4 (SD 11.9) years of age. Presenting clinical features began fewer than 10 days before hospitalization and included abdominal pain, 46 (93.9%); diarrhea, 26 (53.1%); rectal bleeding, 24 (49.0%); and vomiting, 14 (28.6%). Thirty-three patients (67.3%) had prompt abdominal/pelvic CT, in most cases with oral and intravenous contrast media but not timed for optimal arterial visualization; all scans revealed abnormalities typical of colon ischemia,[12] but only 1 report mentioned the status of visceral arteries. Diagnostic evidence comprised colonoscopic[13,14] and biopsy or surgical pathology findings typical of colon ischemia[15] in 40 patients (81.6%); CT and colonoscopic findings typical of colon ischemia without biopsies performed in 7 (14.3%); and CT findings typical of colon ischemia in 2 (4.1%). Comorbid hypertension, hyperlipidemia, nonvisceral vascular disease (coronary, cerebral, or peripheral), diabetes, heart disease, and dialysis dependency were common (Table 1). Twenty-one patients (42.9%) had vascular disease in at least 1 nonvisceral bed. Ten patients (20.4%) were smokers. One patient each had concurrent acute myocardial infarction or bleeding gastric ulcer. RSCI occurred in 43 patients (87.8%) before hospitalization and in 6 (12.2%) during hospitalization after noncolonic surgery: 1 patient each had undergone repair of ruptured abdominal aortic aneurysm, coronary artery bypass grafting, bariatric surgery, lung malignancy resection, subdural hematoma evacuation, or peripheral vascular surgery.

Figure 1 summarizes the treatment and outcome of the 49 patients from the index episode of RSCI to the end of follow-up. Ischemic right colon was

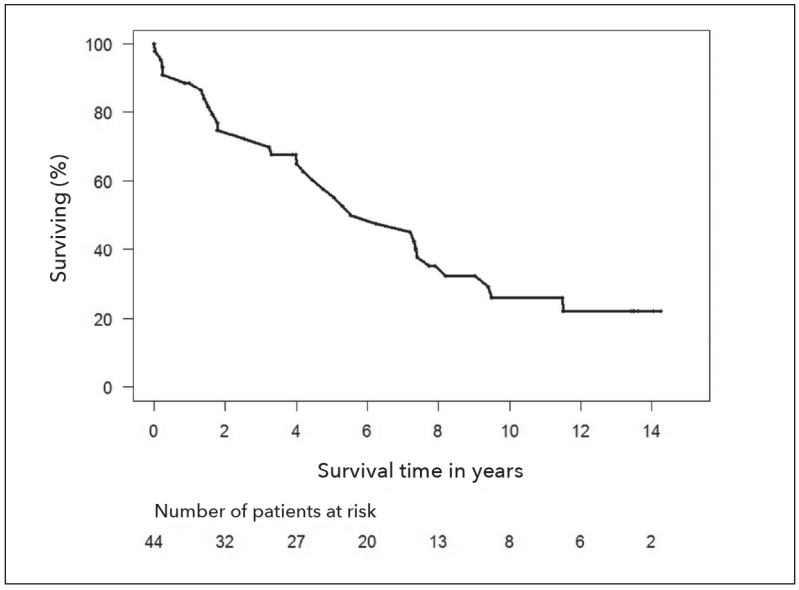

Figure 2. Kaplan-Meier survival curve of 44 patients who survived right-side colon ischemia.

resected in 19 patients (38.8%)—that is, 5 of 6 patients (83.3%) who developed RSCI while receiving postoperative hospital care and 14 of 43 patients (32.6%) who developed RSCI before hospitalization (p value = 0.03). The 19 operated patients comprised 14 of 39 patients (35.9%) with RSCI and 5 of 10 patients (50%) with bilateral ischemia. The procedures were subtotal colectomy in 17 patients, 9 of whom underwent ileostomy, and 1 each who underwent proctocolectomy or total colectomy with ileostomy. All pathologic examinations on resected tissue showed ischemia, but none revealed arteriosclerosis. Four of 19 operated patients (21.1%) died during the index hospitalization, 3 of 5 patients (60.0%) whose RSCI began during postoperative care versus 1 of 14 patients (7.1%) whose RSCI began before hospitalization (p value = 0.04). One nonoperated patient died during the index hospitalization, yielding an overall mortality rate of 10.2%.

We followed the 44 survivors for 5.19 (0.03 - 14.26) years. Nineteen survivors (43.2%) had 1 or more symptomatic vascular disease in a nonvisceral vascular bed before the index episode of RSCI, and 5 of 25 patients (20.0%) who initially had no other vascular disease had the onset of symptomatic nonvisceral vascular disease during follow-up. Therefore, 24 (54.5%) of the survivors had symptomatic nonvisceral vascular disease before or after experiencing RSCI. During follow-up, 4 patients (9.1%) received a cardiac pacemaker for dysrhythmia, and 6 (13.6%) developed malignant tumors: lung cancer, 2; and 1 each with glioblastoma or malignant tumor of the breast, colon, or ureter.

Five patients (11.4%) were diagnosed with symptomatic large visceral artery occlusion, 3 of 15 (20.0%) who had undergone resection of RSCI versus 2 of 29 (6.9%) who had recovered without surgery (p value = 0.32). As shown in Table 2, they manifested abdominal angina preceding RSCI that had been described in outpatient records but remained undiagnosed until after resection (cases 1 and 2), midgut ischemia 1 week after resection (case 3), RSCI 6 weeks after resection of severe left-side colon ischemia (case 4), and abdominal angina beginning more than 3 years after recovery from RSCI without resection (case 5). All had comorbidities, including 4 with nonvisceral vascular disease. After angioplasty and balloon expandable stent placement, none had recurrent mesenteric ischemia until death from another cause (after 1.6 - 7.7 years) or follow-up ended (after ≥ 10 years). The age and proportions that were women or had nonvisceral vascular disease of these 5 patients versus the 39 other survivors were statistically similar: age, 69.6 (SD = 7.5) versus 69.0 (SD = 12.5) years (p value = 0.91); women, 2 (40.0%) versus 26 (66.7%) (p value = 0.34); and nonvisceral vascular disease, 4 (80.0%) versus 15 (38.5%) (p value = 0.15).

Of the 44 survivors of RSCI, 31 (70.5%) died during follow-up or after disenrollment from KP (Figure 1). Twenty-seven (87.1%) died while KP members owing to the following: pneumonia (5); malignant tumor (3); acute myocardial infarction (2); sepsis (2); and 1 each for dementia, pulmonary fibrosis, postcardiac surgery complications, progressive systemic sclerosis, stroke, renal failure, and retroperitoneal abscess; and unknown cause (8). Four patients (12.9%) died after disenrollment; hence, their cause of death was unknown. Therefore, of the 31 patients who died, the cause of death was known for 19 (61.3%); none of them died of mesenteric ischemia. Figure 2 shows the Kaplan-Meier survival curve for the 44 patients who survived the index episode. Estimated survival at 1, 3, 5, and 10 years was 88.6%, 72.3%, 57.6%, and 25.9%, respectively.

DISCUSSION

In this retrospective study, we describe a consecutive series of patients hospitalized with RSCI, including long-term follow-up. Segmental colon ischemia was initially recognized over 50 years ago,[16] and it results from numerous heterogeneous factors.[1,17] More recent studies revealed important distinguishing features of RSCI compared with colon ischemia involving other sites, including the predominance of pain over bleeding,[1] and higher rates of comorbidities, including coronary artery disease,[4,5] atrial fibrillation,[6] and dialysis dependency.[3-6] Patients with extension

… distinguishing features of RSCI compared with colon ischemia involving other sites, including the predominance of pain over bleeding, and higher rates of comorbidities, including coronary artery disease, atrial fibrillation, and dialysis dependency … female predominance …

of RSCI to the left side (bilateral or total colon ischemia) also have higher rates of surgery and mortality.[5,18] The female predominance, vascular and nonvascular comorbidities, and rates of surgery and mortality in our series are similar to the findings in these reports. Notably, rates of surgery and surgical mortality were significantly higher among patients with RSCI that began while they were receiving postoperative hospital care than among those whose RSCI started before hospitalization. As previously reported, right-side or bilateral distribution among various patient characteristics yielded the highest adjusted odds ratio for severe colon ischemia, defined as surgery and/or death.[11] In this series, the 38.8% surgical rate and overall mortality of 10.2% are much higher than rates of 3.3% and 2.7%, respectively, in 368 episodes of non-RSCI treated at the same institution during the same period.[11] Therefore, a role of large artery occlusion in RSCI is plausible compared with the predominant nonocclusive hypoperfusion in patients with ischemia in other locations of the large bowel.[1]

Our most important finding is that 5 patients (11.4%), including 20% of operated cases, had symptomatic large visceral artery occlusion that caused a clinical spectrum comprising abdominal angina preceding RSCI but not diagnosed until after surgical resection (2 cases), midgut ischemia 1 week after resection of RSCI (1 case), RSCI 6 weeks after resection of severe left-side colon ischemia (1 case), and abdominal angina beginning more than 3 years after spontaneous recovery from RSCI (1 case). All were treated with angioplasty

Table 2. Clinical features, therapy, and follow-up of 5 survivors of right-side colon ischemia who had additional mesenteric ischemia because of large visceral artery occlusion

Case	Age,[a] sex	Clinical features and therapy	Chronic comorbidities	Follow-up events
1	73, Female	Postprandial abdominal pain and nausea for 1 year, 7-kg loss RSCI; right hemicolectomy, ileo-colic anastomosis 16 months later abdominal pain persisted, 9-kg loss; abdominal angina identified Catheter angiography: 100% stenosis CA and IMA. 90% stenosis SMA Therapy: SMA ABES	COPD 50 pack/year smoker	Pain stopped,12-kg gain No mesenteric ischemia in 10.2 years to Kaiser Permanente disenrollment
2	70, Male	Postprandial abdominal pain for 2 years RSCI; right hemicolectomy, ileostomy, colon mucus fistula 5 weeks later abdominal pain persisted; abdominal angina identified Catheter angiography: 100% stenoses SMA; tight stenosis CA and IMA Therapy: CA and IMA ABES	COPD Hypertension Peripheral vascular disease 100 pack/year smoker	Pain stopped,10-kg gain Femoral endarterectomy, femoral-anterior tibial bypass No mesenteric ischemia until death from glioblastoma in 1.6 years
3	80, Male	RSCI; right hemicolectomy, ileostomy, colon mucus fistula 1 week later altered mental status, leukocyte count 24,800/mm^3, creatinine 4.5 mg/dL, dusky ileal stoma; mesenteric ischemia suspected Catheter angiography: tight SMA stenosis Therapy: SMA ABES	Type 1 diabetes Hyperlipidemia Coronary artery disease Cerebrovascular disease Atrial fibrillation Congestive heart failure COPD	No mesenteric ischemia until death from COPD in 3.3 years
4	64, Male	LSCI with shock; left hemicolectomy on vasopressors, colostomy stapled Next day "second-look" laparotomy, colostomy matured 6 weeks later RSCI, recovery without surgery Catheter angiography: tight stenoses IMA and SMA Therapy: SMA ABES	Type 2 diabetes Hypertension Hyperlipidemia Coronary artery disease	No mesenteric ischemia until death from myocardial infarction in 7.7 years
5	61, Female	RSCI, recovery without surgery 3.5 years later, onset of postprandial abdominal pain, vomiting, 8-kg loss; abdominal angina identified Catheter angiography: tight stenoses CA, IMA, and SMA Therapy: SMA ABES	Type 1 diabetes Hypertension Hyperlipidemia Coronary artery disease Peripheral vascular disease 50 pack/year smoker	Pain stopped, 9-kg gain No mesenteric ischemia in 10.0 years of Kaiser Permanente follow-up

[a] Age in years at index episode of right-side colon ischemia.

ABES = angioplasty and balloon-expandable stent placement; CA = celiac artery; COPD = chronic obstructive pulmonary disease; IMA = inferior mesenteric artery; LSCI = left-side colon ischemia; RSCI = right-side colon ischemia; SMA = superior mesenteric artery.

and balloon expandable stent placement and had no recurrent mesenteric ischemia until death from nonintestinal disease or at least 10 years of follow-up. Nonvisceral vascular disease was common among all patients with RSCI; 25% of survivors who initially did not have such disease developed it later and there was a trend toward more nonvisceral vascular disease in the 5 patients treated for large visceral artery occlusion than in other patients. Serious cardiac rhythm disturbances and malignant tumors also occurred frequently during follow-up. Overall survival fell progressively for 10 years; 70.4% had died at final follow-up or after disenrollment from KP. Mesenteric ischemia was not diagnosed during follow-up of the other 39 patients or listed as a cause of death in the 61.3% of patients for whom a cause was recorded.

Because the SMA supplies most of the small bowel and the proximal and transverse colon, SMA hypoperfusion with inadequate collateral circulation can cause extensive acute mesenteric ischemia. Poor development of collaterals commonly occurs in the mesentery of the right colon compared with the left side.[2] A pathogenic role of large artery hypoperfusion is manifested when colon ischemia occurs after the IMA is sacrificed during surgery for abdominal aortic aneurysm[19,20] or colon resection,[21] as in case 4 (Table 2), eliminating a critical source of collateral supply to the distribution of a diseased SMA. Therapy of visceral artery occlusion is effective. Patency rates for open revascularization are superior 5 years after treatment; however, postprocedural morbidity and mortality are lower and survival is similar after endovascular treatment.[10]

Our experience expands knowledge on the association between RSCI and large artery occlusion, which is not well described in the literature. In the past, authorities ascribed little role to angiography in colon ischemia,[2] and use of angiography was not reported in more recent descriptions of RSCI.[3-7] Chronic mesenteric ischemia preceding RSCI could have been overlooked because patients with RSCI typically present to Emergency Departments where physicians may focus on their acute symptoms and not recognize previous abdominal angina. A case report describes a 64-year-old American woman who had initial colon ischemia of unstated distribution, subsequent left-side colon ischemia, and previous chronic abdominal pain who underwent stenting of celiac artery and IMA stenoses.She was pain-free 12 weeks later.[22] Another report comments on 2 patients who died of recurrent colon ischemia after arterial stenting for chronic mesenteric ischemia, but clinical, angiographic, and other details are lacking.[23] Some authors now suggest angiography may be useful when acute mesenteric ischemia is also considered in association with colon ischemia or in some cases of RSCI.[24,25] To our knowledge, this is the first detailed report on symptomatic large visceral artery occlusion and its treatment in survivors of RSCI.

The duration of postdischarge follow-up of published series of patients with RSCI was unstated,[3,6,7] or comprised only 30-day[4] or 120-day[5] mortality, limiting identification of subsequent mesenteric ischemia and other events. A recent report on the long-term survival of patients who had undergone surgical resection for colon ischemia at various locations did not assess comorbidities, including mesenteric ischemia, or causes of death.[26] We are unaware of any other detailed long-term outcome studies on RSCI.

A limitation of this study is that we could not assess the usefulness of routine visceral arterial imaging in this study because most of the CT examinations were not properly timed for arterial visualization. Therefore, we have no information on the vascular status of patients who did not undergo angiography. Routine CT angiography could have increased the detection of severe occlusive disease in asymptomatic patients; however, none had mesenteric ischemia diagnosed during long-term observation. Nevertheless, it is possible that the frequency of large-vessel arterial occlusive disease is underestimated in our study. Another limitation is the lack of information on the cause of death in 38.7% of patients, whom we cannot exclude from dying of mesenteric ischemia. Strengths of this study include comprehensive review of outpatient and inpatient records before and after RSCI and prolonged outcome assessment in an integrated health care system.

CONCLUSION

Our experience indicates that physicians should ask patients with RSCI about prior symptoms of abdominal angina (postprandial pain, fear of eating, and weight loss) and that chronic abdominal pain in survivors of RSCI, even beginning years later, should prompt consideration of chronic mesenteric ischemia. Occlusive visceral artery disease should be especially considered in patients who have had surgical sacrifice of the IMA. We support visceral artery imaging by CT angiography routinely during hospitalization for RSCI. The 50% to 100% mortality of acute mesenteric ischemia[8,9] implies that our 5 patients with symptomatic large artery occlusion would have been at high risk if physicians had not identified and treated their disease. CT angiography is accurate,[27] noninvasive, and also useful in initial diagnostic imaging of patients suspected of having RSCI. Visceral duplex scanning[28] and 3-dimensional gadolinium-enhanced magnetic resonance angiography[29] are potential options, depending on local expertise. Catheter angiography confirms disease reported from noninvasive procedures and can be followed by angioplasty and stent placement. Prospective studies are called for to expand knowledge of large-artery visceral disease in RSCI. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Tuning the Harp

The office of medicine is but to tune this curious harp of man's body and to reduce it to harmony.

— Sir Francis Bacon, 1561-1626, English philosopher, statesman, scientist, lawyer, jurist, and author