Aortic clamping during elective operations for infrarenal disease: The influence of clamping time on renal function

Eric Wahlberg, MD, Paul J. DiMuzio, MD, and **Ronald J. Stoney, MD,** *San Francisco, Calif*

Objective: Aortic clamping proximal to the renal arteries is sometimes necessitated during infrarenal and juxtarenal aortic surgery and may be associated with an increased risk of renal ischemia and its consequences. The aim of the study was to estimate this risk and possibly identify a "safe" duration of renal ischemia.

Methods: Medical records were retrospectively reviewed for 60 consecutive patients (from 1987 to 1994) with abdominal aortic aneurysm (n = 43) and occlusive disease (n = 17) confined to the infrarenal or juxtarenal aorta who underwent infrarenal aortic reconstruction with temporary suprarenal clamping. The data obtained included risk factors, preoperative and postoperative serum creatinine level, blood urea nitrogen (BUN) value, proteinuria before surgery, and suprarenal clamping times.

Results: The mean age of the patients was 64.4 years (± 11.4 years), and 74% were men. Concomitant cardiac disease was present in 41% of the patients, and 9% had diabetes. The preoperative creatinine level was 1.21 mg/dL (± 0.54 mg/dL), and the BUN value was 16.6 mg/dL (± 7.8 mg/dL). During surgery, blood flow to the renal arteries was interrupted for 32.0 minutes (± 17 minutes). None of the surviving patients needed dialysis or had signs of acute renal failure after the operations, but transient azotemia (rise in creatinine level) occurred in 23% of the patients. Risk factors for this condition were high preoperative creatinine values and hypotension during surgery, but the main determinant was total renal ischemia time. Odds ratios for such transient renal dysfunction showed as much as a 10-fold risk when suprarenal aortic clamping was greater than 50 minutes as compared with 30 minutes or less.

Conclusion: Postoperative renal function impairment is rare in this group of patients. If suprarenal clamp duration (renal ischemia time) is brief, patients with normal preoperative creatinine levels exhibit no increase or a marginal increase in BUN or creatinine levels after surgery. Accordingly, suprarenal aortic clamping less than 50 minutes in this patient group appears safe and well tolerated. (J Vasc Surg 2002;36:13-8.)

Postoperative renal failure is a known and feared complication after aortic surgery. The incidence rate varies because of the definition of renal dysfunction, but transient nonfatal renal insufficiency occurs in 4% to 5% of patients after aortic surgery for occlusive disease,[1] and a similar incidence rate has been reported for elective infrarenal aortic aneurysm repair.[2] The pathogenesis is multifactorial. Preoperative renal function, the use of nephrotoxic drugs, hypotension, and ligation of the left renal vein during the procedure all negatively affect renal function. Temporary suprarenal aortic clamping causes renal ischemia, and if limb ischemia is also present, it may result in muscle necrosis and myoglobinuria. All these factors combine to cause acute tubular necrosis, resulting in impending or manifest postoperative renal failure.[3] Because the event of a major postoperative complication, such as kidney failure necessi-

tating dialysis, is probably the strongest known predictor of mortality, every possible measure should be taken to minimize that risk during surgery.[4]

Suprarenal aortic clamping is necessitated in about 10% of operations for infrarenal disease, especially when the aneurysm originates close to the renal arteries (juxtarenal).[5,6] Supraceliac aortic clamping via a transcrural approach may avoid dissections of the aortic neck. However, this necessitates two exposures: one supracolic and another infracolic. We prefer pararenal dissection from the infracolic midline for development of circumferential suprarenal exposure to facilitate safe aortic clamp control. We hypothesized if a "safe" suprarenal clamp duration (renal ischemia time) could be determined, the operation during aortic cross clamping could proceed safely and orderly within that time frame. If the duration of cross clamping approached the threshold for renal ischemic injury, measures to minimize damage could be instituted. We suspect that renal ischemic tolerance in patients without other risk factors for kidney failure would be primarily determined by the duration of renal ischemia. The purpose of this study was to evaluate the relationship between postoperative renal function and duration of suprarenal aortic clamping during infrarenal or juxtarenal aortic reconstruction.

MATERIALS AND METHODS

Between January 1988 and June 1994, 120 patients needed aortic clamping above the renal arteries during

Table I. Clinical data and preoperative laboratory values

	Total (n = 60)		AAA (n = 43)		AOD (n = 17)	
	%	(No.)	%	(No.)	%	(No.)
Clinical data						
Associated disease						
CHD	48	(29)	47	(20)	53	(9)
HTN	58	(35)	58	(25)	59	(10)
COPD	22	(13)	23	(10)	18	(3)
Diabetes	10	(6)	7	(3)	18	(3)
Previous vascular surgery						
CABG	7	(4)	7	(3)	6	(1)
CEA	5	(3)	2	(1)	12	(2)
AIBG/AFBG	15	(9)	7	(3)	35	(6)
Infrainguinal	5	(3)		–	18	(3)
Symptoms						
Asymptomatic	53	(32)	74	(32)		–
Claudication	30	(18)	12	(5)	76	(13)
Rest pain	7	(4)	2	(1)	18	(3)
Unknown	10	(6)	12	(5)	6	(1)
Preoperative laboratory values						
Creatinine level						
Total mg/dL mean (range)	1.21	(2.4)	1.27	(2.3)	1.03	(0.9)
<1.25 mg/dL	68	(41)	63	(27)	82	(14)
mg/dL, mean (range)	0.97	(0.6)				
≥1.25 mg/dL	32	(19)	37	(16)	18	(3)
mg/dL, mean (range)	1.71	(1.7)				
BUN						
Total mg/dL, mean (range)	16.6	(29)	17.3	(29)	15.3	(16)
Urinary protein leak						
Negative	31		23		8	
Trace	6		6		–	
30 mg/dL	3		2		1	
300 mg/dL	5		4		1	
Missing data	15		10		5	

CHD, Coronary heart disease; *HTN,* hypertension; *COPD,* chronic obstructive pulmonary disease; *CABG,* coronary artery bypass grafting; *CEA,* carotid endarterectomy; *AIBG/AFBG,* aortoiliac bifurcation graft/aortofemoral bifurcation graft.

procedures performed at the Division of Vascular Surgery, Department of Surgery, University of California, San Francisco. The medical records (except for six that could not be found) for these patients were reviewed regarding indication for surgery, associated disease, type of procedure, and postoperative complications. The analysis also included laboratory data.

Because the study focused on patients with infrarenal aortic disease necessitating clamping above the renal arteries during elective surgery, we excluded all patients with emergent operations (n = 10), graft infection procedures (n = 13), and suprarenal disease (chronic visceral ischemia, n = 22; thoracoabdominal aneurysm, n = 7; celiac artery aneurysm, n = 1; hypoplastic thoracic aorta, n = 1). Patients with known renal disease, renal artery stenosis, or occlusions also were excluded, for a study group of 60 patients.

These patients had a mean age of 64.4 years, ranging from 26 to 82 years at the time of operation, and 44 were men and 16 were women. The indication for surgery was abdominal aortic aneurysm (AAA) for 43 patients and aortoiliac occlusive disease (AOD) for 17. Five cases were reoperations. The most important patient demographics found in the records are presented in Table I. Diseases noted in the records were used for the risk factor categorization. The findings of all patient laboratory evaluations before surgery regarding renal function are presented in Table I. Angiograms (with an unknown contrast load) had been obtained within 14 days before the operation in 62% of the patients (n = 37). With subdivision according to indication, 83% of the patients with AOD and 53% of the patients with AAA had undergone angiography.

Perioperative data. The procedures constituted aortic grafts to the iliac or common femoral arteries, with 38 placed for AAA and 16 for AOD. The remaining procedures were a right aortofemoral graft in a patient with previous amputation (with AOD), one aortic patch (with AAA), and four aortic tube grafts (with AAA). Clamping times and levels of clamping are shown in Table II. *Total renal ischemia time* was defined as the time both renal arteries were clamped. For six patients, the left renal artery was clamped longer than the right. Eighty-seven percent of the patients (n = 52) received mannitol infusion before suprarenal aortic clamping for renal protection. Six patients had *severe hypotension* during surgery, defined as a systolic blood pressure of less than 70 mm Hg for at least 10 minutes. None of the patients had a central venous pressure of less than 2 mm Hg at any period during the operation.

Table II. Intraoperative data on renal artery clamping (n = 60)

	%	(No.)
Aortic clamp level		
Supra renal (immediate)	53	(32)
Supra SMA	20	(12)
Supra celiac	27	(16)
Left renal vein ligation	7	(4)
Renal artery clamping time* (minutes; mean [SD])		
Both arteries	32	(17)
Total left artery	41	(35)
Total right artery	33	(18)

* Renal arteries were clamped separately during operation in six patients. In those patients, clamp was placed completely above renal arteries for some time (both arteries) then moved to occlude only one.
SMA, Superior mesenteric artery; *SD*, standard deviation.

Major intraoperative complications occurred in 11 patients (eight splenic injuries necessitating five splenectomies, two leg ischemia necessitating embolectomy, and one major venous bleeding). Unfortunately, data on blood turnover were not available.

Statistics and definitions. Data are presented as mean, standard deviation, standard error, or frequency. According to Johnston and Scobie,[5] a serum creatinine level of less than 1.25 mg/dL was considered normal, and *transient postoperative renal insufficiency* was defined as a rise in creatinine level or blood urea nitrogen (BUN) value of 20% of the preoperative value. Negative proteinuria and traces of preoperative proteinuria were regarded as *absence of protein leak*. Calculations and comparisons were performed with the laboratory values at postoperative day 4 because the values peaked at day 3 or 4 for creatinine level and at day 4 or 5 for BUN value (Fig 1).

Linear regression was used to determine the relationship between variables, and standard univariate methods (Student *t* test or Yates corrected χ^2 test) were used to identify predictors of transient renal insufficiency. Differences were considered significant when the *P* value was less than .05.

RESULTS

Two patients died within 30 days of the operation, one of stroke on postoperative day 17 and one of visceral ischemia on postoperative day 5, for a mortality rate of 3.5%. Both patients were included in the analysis. Postoperative complications included four cases of respiratory failure, two cases of paraplegia, and one case each of pneumonia, colon ischemia, leg ischemia, and bleeding.

Postoperative renal function. Except for the patient who died with visceral ischemia and had highly elevated creatinine values during the postoperative period (5 days), no other patients had postoperative acute renal failure or tubular necrosis. However, as a group, the patients had an immediate rise in creatinine level and a delayed increase in BUN value, both of which were significant (*P* < .01). The values were normalized at discharge (Fig 1). The creatinine
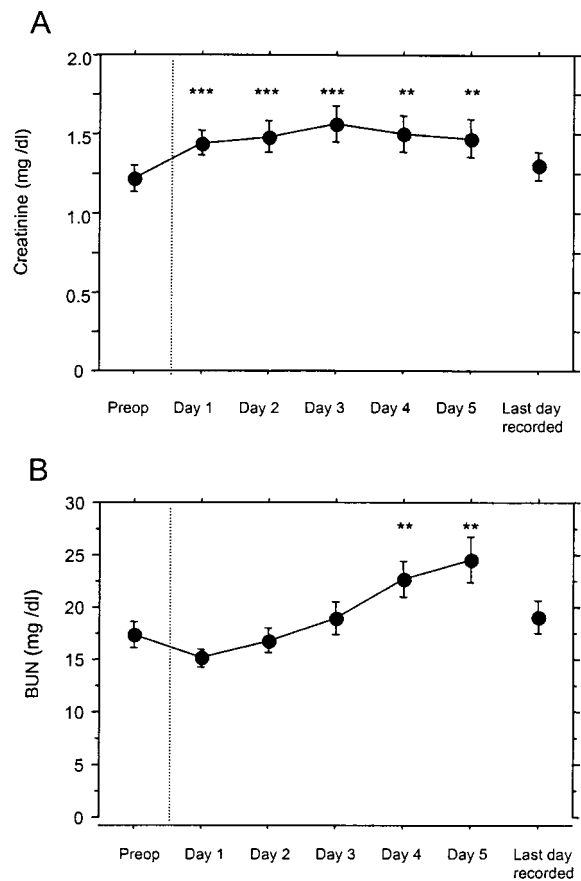

Fig 1. Creatinine **(A)** and BUN **(B)** values before and after operation (mean and standard error; n = 60).
**P < .01 compared with preoperative values according to Student *t* test.
***P < .001 compared with preoperative values according to Student *t* test.

level elevation was at least 20% more than preoperative values in 18 patients (30%), and 21 patients (35%) had BUN values increased to the same magnitude at postoperative day 4. The 14 patients (23%) with a 20% increase in both values at postoperative day 4 or 5 were classified as having transient renal insufficiency and were compared with the patients without a 20% rise over preoperative values in the subsequent analyses (Fig 2).

Differences between groups. The two compared groups were similar for gender, mean age, and presence of chronic obstructive pulmonary disease, diabetes, hypertension, and peripheral vascular disease. A tendency was seen in that patients in whom transient renal insufficiency developed commonly had a history of atherosclerotic heart disease (*P* = .07) and a preoperative creatinine level of more than 1.25 mg/dL (*P* = .10). No difference between the groups was found regarding presence of preoperative proteinuria or frequency of angiography. The group with elevated creatinine and BUN values on day 4 tended to
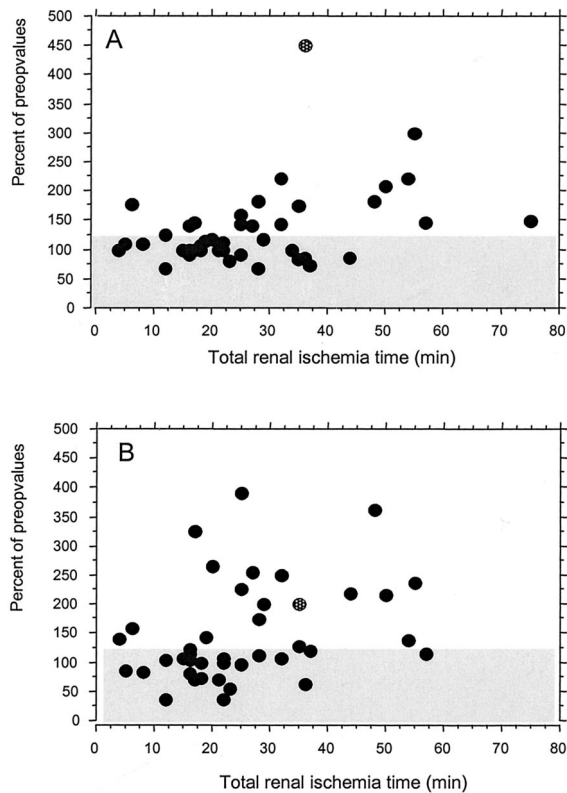
Fig 2. Percent of preoperative values at day 4 in creatinine **(A)** and BUN **(B)** plotted against time both renal arteries were clamped. *Patterned symbol* represents patient who died day 5 as result of visceral ischemia. *Shadowed parts* of graphs represent patients without transient renal insufficiency (n = 57).

Table III. Univariate analysis of risk factors possibly associated with development of transient renal insufficiency

Variable	Creatinine level P value	BUN P value
Preoperative		
Age	.599	.593
Sex	.225	.108
Indication (AAA/AOD)	.760	.390
Hypertension	.212	.947
Atherosclerotic heart disease	.523	.121
Chronic obstructive pulmonary disease	.665	.064
Peripheral vascular disease	.284	.548
Diabetes mellitus	.514	.376
Angiogram	.166	.079
Creatinine level >1.25 mg/dL	.014	.049
Urinary protein leak	.154	.716
Intraoperative		
Renal ischemia time	.0001	.0002
Clamp level	.364	.702
Ligated left renal vein	.755	.251
Hypotension	.075	.028
Kidney protection	.281	.831
Major complication	.775	.158

P value for H_0: no association between variable and creatinine and BUN values at postoperative day 4.

more often have hypotension ($P = .09$) during the operation, but no difference in the numbers of ligated left renal veins and other major complications was found. The groups also had similar numbers of missed renal protection with mannitol.

Although the clamp levels were similar for both groups, the total renal ischemia times were significantly ($P = .013$) longer for patients with creatinine and BUN value elevations compared with those without (Fig 2). This was even more apparent in comparison of the left renal artery clamping time for the groups ($P = .002$).

Prediction of transient renal insufficiency. Risk factors that predicted transient renal insufficiency were total renal ischemia time ($r = 0.57; P < .001$) and a preoperative creatinine level of more than 1.25 mg/dL ($r = 0.30; P = .02$), and the occurrence of intraoperative hypotension tended ($r = 0.27; P = .07$) to be related to elevated creatinine values at day 4 (Table III). However, elevated BUN values at day 4 were clearly related to total renal ischemia time ($r = 0.55; P < .001$) and a preoperative creatinine level of more than 1.25 mg/dL ($r = 0.36, P = .04$) and intraoperative hypotension ($r = 0.34; P = .03$). A possible relationship also was found between high BUN

values at day 4 and chronic obstructive pulmonary disease ($r = 0.33; P = .06$). When the previously mentioned risk factors were evaluated with the stepwise regression model, only total renal ischemia time was identified as an independent risk factor for postoperative rise in BUN value ($r = 0.55; P < .001$). For elevated creatinine level, total renal ischemia time ($r = 0.57; P < .0001$) and a preoperative value of more than 1.25 mg/dL ($r = 0.64; P < .001$) contributed to the model. Odds ratios for transient renal insufficiency for different clamping times are shown in Table IV.

DISCUSSION

This study supports the concept of suprarenal aortic clamping when necessitated to manage juxtarenal or pararenal aortic reconstructions.[1,7-9] Only one patient who died after surgery needed dialysis, and only 23% of the patients had elevated creatinine and BUN values more than 20% over preoperative values at the peak on postoperative day 4.

Our primary goal was to select a group of patients without other renal risk factors and determine whether the duration of aortic clamping influenced postoperative renal function. In addition, we also hoped to define a "safe" (tolerable) duration of renal ischemia. For enough patients in the study group, joint analysis of patients with AAA and AOD was necessitated, which makes direct comparisons with other studies difficult. However, overall mortality figures and the extent of other risk factors among the patients were comparable with previously published data.

Table IV. Estimated odds ratio *(OR)*, confidence interval *(CI)*, and *P* value for developing transient renal insufficiency

Clamping time	Total 57*	Yes 21	No 36	Risk versus 0-25 minutes			Risk versus 26-50 minutes		
				OR	CI	P	OR	CI	P
0-25 min	28	6	22	–	–	–	–	–	–
26-50 min	23	10	13	2.2	0.5 - 8.8	.13	–	–	–
51+ min	6	5	1	12.0	1.0 - 141.3	.01	5.5	0.6 - 65.1	.19

Transient renal insufficiency defined as increase in BUN and creatinine level > 20% compared with preoperative values.
* Three patients without available laboratory values at day 4 are excluded from analyses.

Our 30-day mortality rate of 3.5% is almost identical to earlier reports, with rates between 3% and 7%, for patients needing aortic clamping above the renal arteries for AAA.[6,8,10] For AOD, no publications exist to our knowledge that focus on clamping above renal arteries for elective cases. Mortality rates around 5% are common in reports on patients with clamping both above and below the renal arteries.[11] Demographics of our group of patients are also similar to earlier published data.[8,9,12]

The selected patients represent a group with aortic disease close to the renal arteries that need special technical solutions during surgery. This also, at least partly, explains the rather high incidence rate of splenic injuries and the two cases of mild paraplegia that occurred. The latter two patients both underwent urgent surgery for AAA, and both had clamping just above the renal arteries with clamping times of 47 and 22 minutes. Another possible contributing factor was a major vein bleeding that complicated one of the operations.

Our study differs from other studies in several aspects. The first difference is the clamping level. Most articles present a majority of clamps placed at the supraceliac level, but in our study, most patients underwent aortic clamping immediately above the renal arteries.[6,9] The reason for this difference is preference. If aortic clamping is necessitated above the renal arteries to reconstruct occlusive or aneurysmal disease, we prefer the segment of the aorta that is normal and closest above the renal artery origin (suprarenal), followed next by supramesenteric, and lastly supraceliac. Clamping immediately above the renal arteries is thought by some investigators to be associated with a higher risk for postoperative renal failure because of renal atheroembolization from juxtarenal atherosclerotic lesions.[2,6] We were not able to confirm such a relationship in this study, and postoperative laboratory data on renal function were similar for patients with clamping at different levels. Thorough mobilization of the aorta and renal arteries before clamping is safe in our experience and supported by our low rate of transient renal dysfunction. Another difference from other studies is that the renal vein was ligated in only 7% of our patients as compared with other studies that report a 3% to 10% incidence rate for aortic operations for AAA where most patients had clamping below the renal arteries.[13,14]

Our results, which include data from the one patient who died of visceral ischemia with renal insuffiency, are equal to previous data reported from comparable patient groups. Of 41 patients with AAA, with 30 supraceliac and 11 suprarenal aortic clamps, Green et al[6] reported three patients who needed dialysis. Breckwoldt et al[8] reported 39 patients with AAA who needed aortic clamping above the renal arteries and only one patient with dialysis after surgery. This dialysis incidence rate is low compared with operations for thoracoabdominal aneurysms that often have rates around 6% to 7%.[15,16] The low incidence rate makes dialysis an imprecise endpoint when studying postoperative renal function after high aortic clamping.

We therefore have to rely on laboratory data on renal function, as have other investigators. Both creatinine and BUN values are influenced in the early postoperative period to a large extent by the degree of tissue catabolism, and the levels are more affected by critical illness than renal function. Serum BUN levels are influenced by patient hydration and urinary output and glomerular filtration rate. Creatinine levels also are determined by the amount of muscle mass but are a better index of glomerular filtration rate. An increase in creatinine level may therefore be a more reliable predictor of deteriorated renal function per se, and BUN elevation may also mirror the function of other organs. The rise in BUN values we observed may reflect more the general complication rate after operation rather than actual renal dysfunction. Nevertheless, the magnitude of increase is influenced by renal function to some extent, especially in the absence of major postoperative complications. We chose the criteria of Scobie and Johnston[5] as an endpoint as have other investigators.[8] Such transient, laboratory-derived, renal insufficiency occurs in 3% to 30% of patients after aortic clamping above the renal arteries.[5,6,8,12] The choice of criteria and what parameters are chosen as endpoints cause the variability in frequency.

In spite of our goal, total renal ischemia time was not the only variable that was related to transient renal insufficiency. Not surprisingly, it was significantly related to two risk factors: a preoperative creatinine level of more than 1.25 mg/dL and intraoperative hypotension. Both findings are consistent with series on consecutive elective AAA repair with clamping below the renal arteries.[2,12] If the preoperative creatinine level was less than 2 mg/dL, only 5% of more than 600 patients with AAA had increased creatinine levels more than 20% after surgery and only 0.4% needed dialysis. The dialysis rates were much higher when the preoperative creatinine level was between 2 and 4

mg/dL.[2] This observation for patients needing temporary aortic clamping above the renal arteries is supported by a study of Crawford treating juxtarenal aneurysms[17] and this study. Breckwoldt et al[8] were unable to identify any specific risk factor predicting transient renal insufficiency for patients needing suprarenal aortic clamping.

The main determinant of the levels of BUN and creatinine after surgery was the clamp duration (renal ischemia time) in this study. We found a strong relationship to the laboratory value per se, and a highly significant difference between the groups with and without transient renal ischemia was seen. In the stepwise regression analysis, it was the only component contributing to the model of predicting transient renal insufficiency on the basis of BUN values. A preoperative creatinine level of more than 1.25 mg/dL also predicted a postoperative rise in creatinine level in addition to a long clamping time. Our estimation of odds ratios for development of transient renal insufficiency on the basis of aortic clamp duration could probably be considered relevant. The estimations suggest that the risk is extremely low for total renal ischemia time less than 25 minutes and only slightly higher when clamping time is less than 50 minutes. The confidence intervals were, however, rather large for the latter prediction. A safe renal ischemia time of 60 minutes is supported experimentally[18] and in clinical studies,[7,8,17] with ischemia up to 100 minutes regarded as safe.[19]

CONCLUSION

Postoperative renal failure is unusual after temporary suprarenal aortic clamping during an elective aortic reconstruction in patients with infrarenal aortic disease. If the aorta is clamped less than 25 minutes, even marginal postoperative elevations in BUN or creatinine levels are extremely rare. The risk for transient renal insufficiency is doubled when the aorta is clamped 25 to 50 minutes and 10 times as great when the clamping time exceeds 50 minutes. This risk is the same for varied clamping levels above the renal arteries. Accordingly, aortic clamping above the renal arteries for up to 50 minutes in this patient group seems safe and should not be ignored as an option for avoidance of renal insufficiency.

REFERENCES

1. Diehl J, Cali R, Hertzer NR, Bevin EG. Complications of abdominal aortic reconstruction: an analysis of perioperative risk factors in 557 patients. Ann Surg 1983;197:49-56.

2. Johnston K. Multicenter prospective study of non-ruptured abdominal aortic aneurysm. Part II. Variables predicting morbidity and mortality. J Vasc Surg 1989;9:437-47.

3. Rosen S, Heyman SN. Difficulties in understanding human "acute tubular necrosis": limited data and flawed animal models. Kidney Int 2001;60:1220-4.

4. Gornick C, Kjellstrand C. Acute renal failure complicating aortic aneurysm surgery. Nephron 1983;35:145-57.

5. Johnston K, Scobie T. Multicenter prospective study of non-ruptured abdominal aortic aneurysm. Part I. Population and operative management. J Vasc Surg 1988;7:69-81.

6. Green R, Ricotta J, Ouriel K, DeWeese J. Results of supraceliac clamping in the difficult elective resection of infrarenal abdominal aortic aneurysm. J Vasc Surg 1989;9:125-34.

7. Joyce W, Ward A. Supraceliac clamping: an underused alternative in aortic surgery. Ann Vasc Surg 1990;4:393-6.

8. Breckwoldt W, Mackey W, Belkin M, O'Donnell T. The effect of suprarenal cross-clamping on abdominal aortic aneurysm repair. Arch Surg 1992;127:520-4.

9. Schneider J, Gottner R, Golan J. Supraceliac versus infrarenal aortic cross-clamp for repair of non-ruptured infrarenal and juxtarenal abdominal aortic aneurysm. Cardiovasc Surg 1997;5:279-85.

10. Faggioli G, Stella A, Freyrie A, Gargiulo M, Tarantini S, Rodio M, et al. Early and long-term results in the surgical treatment of juxtarenal and pararenal aortic aneurysms. Eur J Vasc Endovasc Surg 1998;15:205-11.

11. Szilagy D, Eliott J, Smith R, Reddy D, McPharlin M. A thirty-year survey of the reconstructive surgical treatment of aortoiliac occlusive disease. J Vasc Surg 1986;3:421-36.

12. Martin L, Atnip R, Holmes P, Lynch J, Thiele BL. Prediction of postoperative complications after elective surgery using stepwise logistic regression analysis. Am Surg 1984;60:163-9.

13. Adar R, Rabbi I, Bass A, Papa M, Schneiderman J, Walden R. Left renal vein division in abdominal aortic aneurysm operations. Arch Surg 1985;120:1033-6.

14. Calligaro K, Savarese R, Combs P, DeLaurentis D. Division of the left renal vein during aortic surgery. Am J Surg 1990;160:192-6.

15. Schepens MAAM, DeFauw JAM, Hamerlijnck RPH, DeGeest R, Vermeulen FEE. Surgical treatment of thoracoabdominal aortic aneurysms by simple cross-clamping. J Thorac Cardiovasc Surg 1994;107:134-42.

16. Kashyap VS, Cambria RP, Davidson K, L'Italien GJ. Renal failure after thoracoabdominal aortic surgery. J Vasc Surg 1997;26:949-57.

17. LeMaire SA, Miller CC, Conklin LD, Schmittling ZC, Köksoy C, Coselli JS. A new predictive model for adverse outcomes after elective thoracoabdminal aortic aneurysm repair. Ann Thorac Surg 2001;7: 1233-8.

18. Krause SM, Walsh TF, Greenlee WJ, Ranaei R, Williams DL Jr, Kivilighn SD. Renal protection by a dual ETa/ETb endothelin antagonist L-754,142, after aortic cross-clamping in the dog. J Am Soc Nephrol 1997;8:1061-71.

19. Kiley J, Poweres S, Beebe R. Acute renal failure. Eighty cases of renal tubular necrosis. N Engl J Med 1960;262:481-6.