Myocardial injury in major aortic surgery

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Purpose: The purpose of this study was to examine the effects of major aortic surgery and its associated oxidative stress and injury on the myocardium.
Methods: Plasma from 27 patients who underwent thoracoabdominal aortic aneurysm (TAAA) repair and 17 patients who underwent infrarenal aortic aneurysm (AAA) repair was collected at incision, aortic crossclamping, and reperfusion and 1, 8, and 24 hours thereafter. Samples were assayed for the myocardial specific protein troponin-T, total antioxidant status, and lipid hydroperoxides.
Results: Ten patients experienced cardiac dysfunction in the first 24 hours after surgery (eight patients in the TAAA group and two patients in the AAA group). Immediately after reperfusion, total antioxidant status levels dropped in all patients with TAAA and with AAA; this was more marked in patients with TAAA, leading to a significant difference between the two groups at this time point and for up to 1 hour thereafter ($P < .01$). Patients with TAAA showed a sharp rise in lipid hydroperoxide levels immediately after reperfusion, and levels were significantly higher than in patients with AAA ($P = .0007$). In patients with AAA, no significant change in troponin-T was observed throughout the study period; whereas in patients with TAAA, levels were significantly elevated at 8 and 24 hours after reperfusion ($P < .01$). Troponin-T levels significantly correlated with total antioxidant status ($r = –0.5$) and lipid hydroperoxides ($r = 0.78$) but not with systolic blood pressure.
Conclusion: Supracoeliac aortic crossclamping is associated with a significant release of the myocardial injury marker troponin-T. This seems to correlate with the severity of oxidative rather than hemodynamic stresses. Ameliorating oxidative injury during TAAA surgery may therefore have a cardioprotective effect. (J Vasc Surg 2000;31:742-50.)

During aortic aneurysm surgery, the myocardium is subjected to considerable mechanical and biochemical stresses. The incidence of postoperative myocardial infarction (MI) after supraceliac clamping for thoracoabdominal aortic aneurysm (TAAA) surgery is reported to be between 4% and 7%, whereas that for postoperative cardiac complications without evidence of ischemic damage is between 12% and 36%.[1-4] These non-MI cardiac complications may manifest as pulmonary edema, newly developed arrhythmias, or diminished cardiac output in the absence of an obvious cause. The development of these complications after major surgery may adversely affect recovery in the immediate postoperative period and is also associated with significantly increased risk of cardiovascular death in the long term.[5] Although mechanical stress to the myocardium can lead to cardiac damage, another possible mechanism is remote injury as the result of ischemia-reperfusion.

Tissue injury after ischemia-reperfusion is a clinical situation in which excessive oxygen-derived free radical (ODFR) production is thought to play an important role, particularly after intestinal ischemia-reperfusion.[6] ODFRs are highly reactive radicals that can react with any chemical in their environment. To protect against the destructive effects of ODFR, an elaborate free radical scavenging system exists. This antioxidant system is made of specific intracellular antioxidant enzymes and of free circulating plasma antioxidants.[7] Measurement of changes to the plasma antioxidant capacity provides an indirect method of quantifying global oxidative stress.[8]

One of the main sites of ODFR action is the cell wall membrane. On exposure to ODFR, the polyunsaturated fatty acids present in the cell wall undergo lipid peroxidation.[9,10] Lipid peroxidation of cellular membranes is associated with a multitude of functional changes, ranging from decreased fluidity to loss of selective permeability and signal transduction.

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Competition of interest: nil.
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0741-5214/2000/$12.00 + 0 24/1/102325
doi:10.1067/mva.2000.102325

In this study, we evaluated myocardial damage associated with reperfusion after supraceliac and infrarenal aortic crossclamping by measuring changes to the myocardium-specific protein troponin-T (TnT). This protein is a sensitive and specific marker for myocardial injury.[11,12] We also studied the relationship between TnT changes and the magnitude of oxidative stress and oxidative injury as measured by changes to the total plasma antioxidant status (TPAS) and lipid hydroperoxide (LHP), respectively.

PATIENTS AND METHODS

With approval by the ethics committee, informed consent to participate in the study was obtained from 27 patients who were undergoing elective Crawford types III and IV[13] TAAA repair and 17 patients undergoing elective infrarenal abdominal aneurysm (AAA) repair. In our institution, Crawford types III and IV TAAA are repaired with simple supraceliac aortic crossclamping without shunting or left heart bypass grafting. Ventricular function in all patients who underwent elective TAAA surgery was assessed before the operation by stress echocardiography, as previously described.[14,15] Only patients with no significant coronary artery disease (ventricular wall motion score, 16-18)[14] were included in this study. Physiologic status before and after the operation was evaluated with the Acute Physiology and Chronic Health Evaluation II score (APACHE II).[16] For the purpose of this study, postoperative cardiac dysfunction was identified as the occurrence of one or more cardiac events, excluding MI. These events included newly developed arrhythmias (arrhythmias requiring pharmacologic correction), electromechanical dissociation (sudden disappearance of an effective arterial pressure in the presence of adequate electrocardiographic complexes), and cardiac arrest. Patients with AAA were assessed clinically before the operation, and all patients underwent preoperative electrocardiography. Once deemed clinically fit for surgery, patients with AAA had no further cardiac investigations for occult coronary artery disease.

After induction of anesthesia, a radial arterial line was inserted, and arterial samples were collected at incision, on aortic clamping (supraceliac in patients with TAAA and infrarenal in patients with AAA), on reperfusion (splanchnic in patients with TAAA and limb in patients with AAA), and at 1, 8, and 24 hours after reperfusion. Plasma was separated immediately, snap frozen, and later assayed for changes to TPAS with the use of the Randox assay[17] (Randox Laboratories, Co.Antrim, UK), for changes to LHP with the use of the Peroxoquant assay[18] (Pierce & Warriner, Chester, UK), and for the myocardial specific protein TnT[19] (Boheringer Mannheim, Lewes, UK). After the operation, patients with TAAA were admitted to the intensive therapy unit although most of the patients with AAA were admitted to a high-dependency unit. The monitoring modalities in these two units are identical; the only difference is that the high-dependency unit does not have the facility for mechanical ventilatory support. All patients received continuous electrocardiography and arterial pressure and central venous pressure monitoring after the operation. In addition, patients with TAAA had pulmonary artery pressures monitoring.

Normality tests were performed on all data. For nonparametric data, the median figures were used, and statistical analysis between groups was performed with the Mann-Whitney *U* test corrected for ties and for repeated measurements (Bonferroni). Statistical analysis between time points within the same group was performed with the Wilcoxon signed ranks test. The Student *t* test and Fisher's exact test were used in risk factor analysis. Data related to arterial pressures, heart rates, and APACHE II score were parametric and are presented as mean and were analyzed with the analysis of variance test. Statistical significance was assumed when probability values were less than .01 for all tests.

RESULTS

In patients with TAAA, the median preoperative stress ventricular wall motion score was 16 (range, 16-18) in both groups of patients with and without postoperative cardiac dysfunction. Table I shows the demographic data for the patients included in this study. Patients with TAAA had a median age of 69 years (range, 50-80 years), whereas patients with AAA had a median age of 76 years (range, 53-84 years; $P = .005$). Patients with TAAA had significantly longer distal (lower limb) ischemia time and had significantly more blood transfusions between operations. Table II shows the distribution of cardiac events in all patients. Of the 44 patients studied, 10 patients experienced the development of cardiac dysfunction in the first 24 hours after surgery (eight patients in the TAAA group and two patients in the AAA group). Another two patients in the TAAA group experienced the development of transmural MI after the operation and were excluded from the study. The median time of cardiac complication occurrence was 4 hours (range, 1-24 hours) postperfusion.

The incidence of major postoperative complications (death, renal failure requiring hemofiltration, and respiratory failure requiring ventilation for 4 or

Table I. Demographic and risk factor analysis of patients included in the study

Variable	*TAAA*	*AAA*	P *value*
Patients (n)	27	17	
Women / men (n)	9 / 18	5 / 12	
Median age (y; range)	69 (50-80)	76 (53-84)	.005*
Crawford type III (n)	15	—	
Crawford type IV (n)	12	—	
Smoker (n)	10	6	.6†
Hypertension (n)	15	8	.5†
Median visceral ischemia time (min; range)	43 (11-122)	—	
Median distal ischemia time (min; range)	68 (30-160)	52 (30-115)	.01*
Median intraoperative blood transfused (units; range)	10 (2-35)	6 (1-8)	.001*

*t Test.
†Fisher exact test.

Table II. Distribution of postoperative cardiac complications

Cardiac event	*TAAA (n = 27 patients)*	*AAA (n = 17 patients)*
MI (n)	2	—
Cardiac arrest / electro-mechanical dissociation (n)	4	—
Arrhythmia* (n)	4	2
TOTAL (n)	10	2

*All were atrial fibrillation.

Table III. Distribution of major complications in patients with TAAA based on cardiac outcome

Cardiac outcome	*With cardiac dysfunction (n = 8)*	*Without cardiac dysfunction (n = 17)*	P *value**
Respiratory failure	4	3	.1
Renal failure	4	5	.2
Death	4†	2‡	.05

*x^2 Test.
†Two patients died of cardiac arrest, and two patients died of coagulopathy.
‡Both patients died of coagulopathy.

more days) was 87.5% in the group with cardiac dysfunction and 47% in the group with no complications (P = .03, Fisher's exact test). Table III shows the distribution of these complications.

Table IV shows the demographic and risk factor analysis of patients with TAAA, based on the presence of postoperative cardiac dysfunction. No significant difference in ischemia time or other risk factors was found between the two groups.

Table IV. Demographic and risk factor analysis of patients with TAAA based on the development of cardiac dysfunction

Variable	*Without dysfunction*	*With dysfunction*	P *value*
Patients (n)	17	8	
Median age (y; range)	70 (62-80)	64 (50-76)	.1*
Median visceral ischemia time (min; range)	44 (11-68)	43 (18-122)	.42*
Median distal ischemia time (min; range)	72.5 (46-148)	84 (40-160)	.26*
Median intraoperative blood transfused (units; range)	10 (2-35)	11.5 (6-19)	.82*
Smoker (n)	6	4	.4†
Hypertension (n)	8	7	.6†

*Two independent sample t-test; two-tailed P value.
†Fisher exact test.

Systemic and arterial pressures and heart rate. There was no significant difference between patients with TAAA with or without cardiac complications in any of these parameters at any of the time points. In all, eight patients with TAAA required inotrope support immediately after splanchnic reperfusion. Three of these patients were in the group with cardiac complications.

APACHE II scores. Fig 1 shows the APACHE II scores for patients with TAAA, based on their cardiac outcome. There was no significant difference between preoperative scores and scores recorded on admission to the intensive care unit between these two groups of patients.

However, patients who went on to experience the development of cardiac dysfunction had significantly higher scores from day 1 to day 4 after the operation. Most patients who had no cardiac complications were discharged from the intensive care unit after 4 days.

TPAS. TPAS levels (Fig 2) were not significantly different between patients with TAAA and patients with AAA at the incision and aortic cross-clamping time points. Immediately after reperfusion, a drop in TPAS level was observed in both groups; this was more marked in patients with TAAA, leading to a significant difference between the two groups at this time point (P = .0005). At 1 hour after reperfusion, levels were still significantly lower in patients with TAAA (P = .005). Recovery of TPAS levels occurred between the 1 and 8 hours after reperfusion time points, and no significant difference between the two groups of patients was observed at 8 and 24 hours after reperfusion.

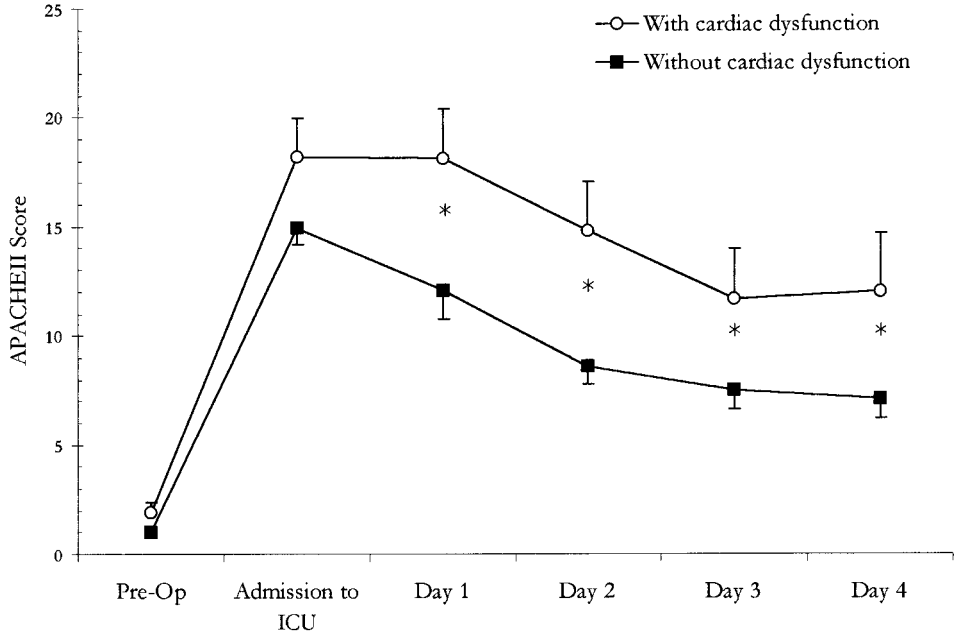

Fig 1. Mean APACHE II score values in patients with TAAA based on their cardiac outcome. Eight patients experienced postoperative cardiac events, and 17 patients did not. $^{*}P < .01$, analysis of variance.

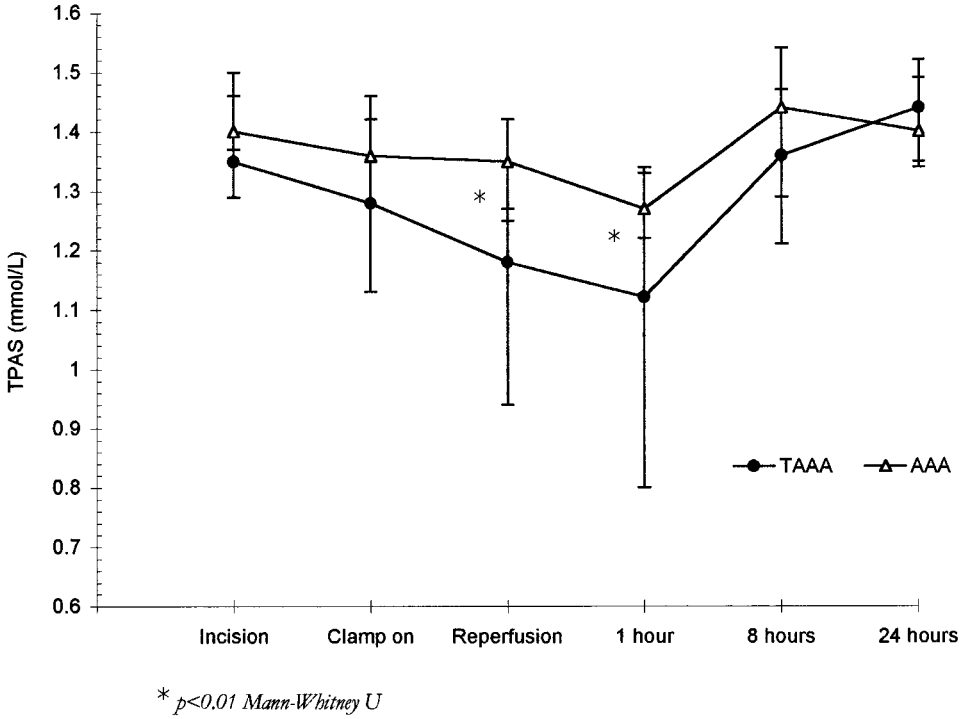

Fig 2. TPAS in patients with TAAA and in patients with AAA. Data represent median, (interquartile range).

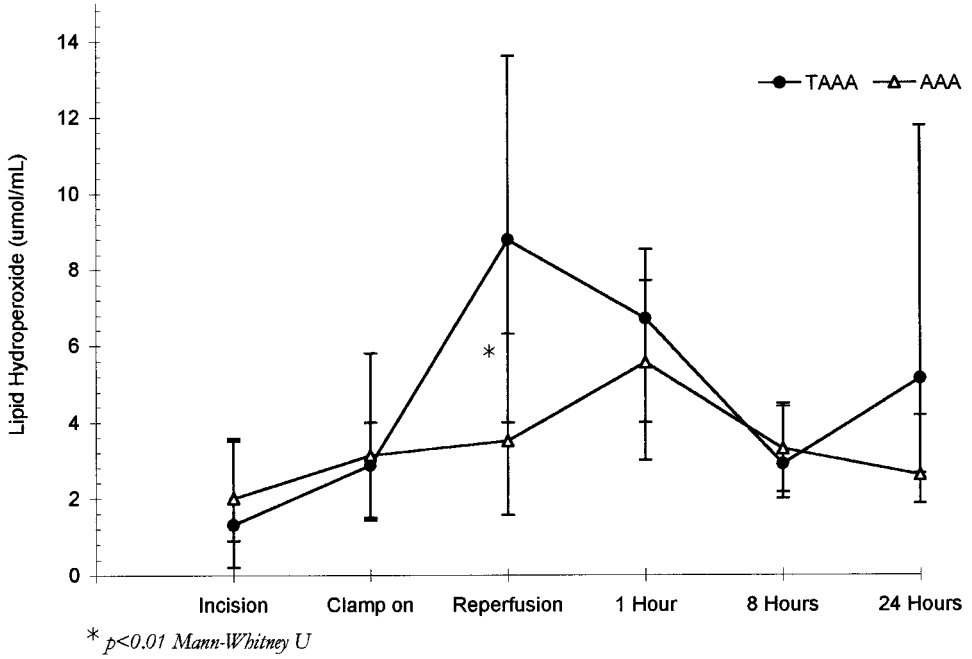

Fig 3. LHP changes in patients with TAAA and in patients with AAA. Data are presented as median (interquartile range).

Plasma LHP. Fig 3 shows the changes in LHP levels in patients with TAAA and in patients with AAA. Levels were also not statistically significant between the two groups at incision and crossclamping time points. Immediately on reperfusion, LHP levels showed a sharp rise in patients with TAAA, and a significant difference between the two groups was observed at this time point ($P = .0005$).

TnT. Fig 4 shows TnT changes in patients with TAAA and in patients with AAA. At incision, the median TnT value was 0.01 ng/mL (range, 0.0-0.02 ng/mL) in both groups. In patients with AAA, no significant change in TnT levels was observed throughout the study period; whereas in patients with TAAA, TnT levels increased to 0.07 ng/mL (0.03-0.08 ng/mL) at 8 hours and 0.04 ng/mL (0.02-0.1 ng/mL) at 24 hours after reperfusion ($P < .01$, both points). Values in patients with TAAA were significantly higher than those values in patients with AAA at 8 and 24 hours after reperfusion ($P < .01$, both points).

Fig 5 shows the changes of TnT levels in patients with TAAA, based on the presence or absence of cardiac dysfunction. In the eight patients with TAAA who experienced postoperative cardiac dysfunction, TnT levels showed a stepwise elevation reaching a maximum of 0.1 ng/mL (0.03-0.21 ng/mL) at 24 hours after reperfusion. TnT levels in this group were significantly higher than those levels in patients without cardiac complications at 1, 8, and 24 hours after reperfusion ($P < .01$, all time points). In the two patients with TAAA who were excluded from the study and who sustained MI, peak TnT levels were nearly tenfold higher than those levels measured in patients with cardiac dysfunction.

Spearman's linear correlation analysis revealed a significant correlation between peak TnT levels and each of the lowest TPAS ($r = –0.5$; $P = .01$) and peak LHP levels ($r = 0.57$; $P = .01$). There was no significant correlation between TnT levels and duration of splanchnic or total ischemia times. With the use of the same analysis, there was a significant correlation between visceral ischemia time and LHP levels ($r = 5.1$; $P = .01$) but not with TPAS levels ($r = –0.2$; $P = .1$). TPAS baseline levels of less than 1.4 mmol/mL correlated significantly with the development of postoperative complications ($P = .01$, Fisher exact test).

Multiple regression analysis after correction for ischemia time and blood transfusion showed no correlation between peak TnT levels and lowest recorded systolic blood pressure (lowest pressure reading lasted for 10 minutes or more during and after surgery; $r = –0.03$; $P = .9$). However, a significant

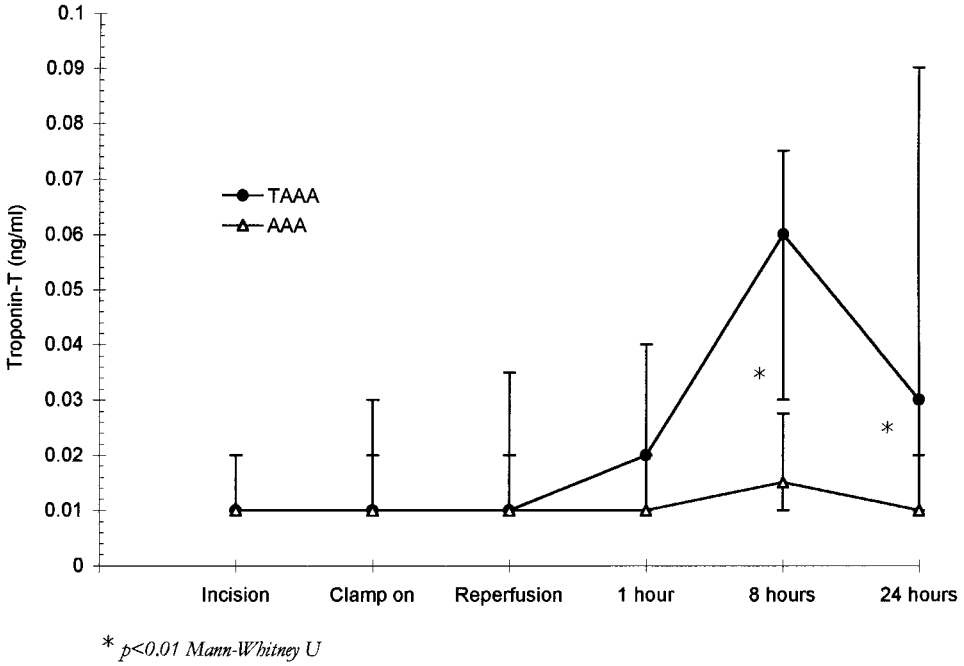

Fig 4. Changes in plasma TnT levels in 25 patients with TAAA (after two patients with postoperative MI were excluded) and in 17 patients with AAA. Data are presented as median.

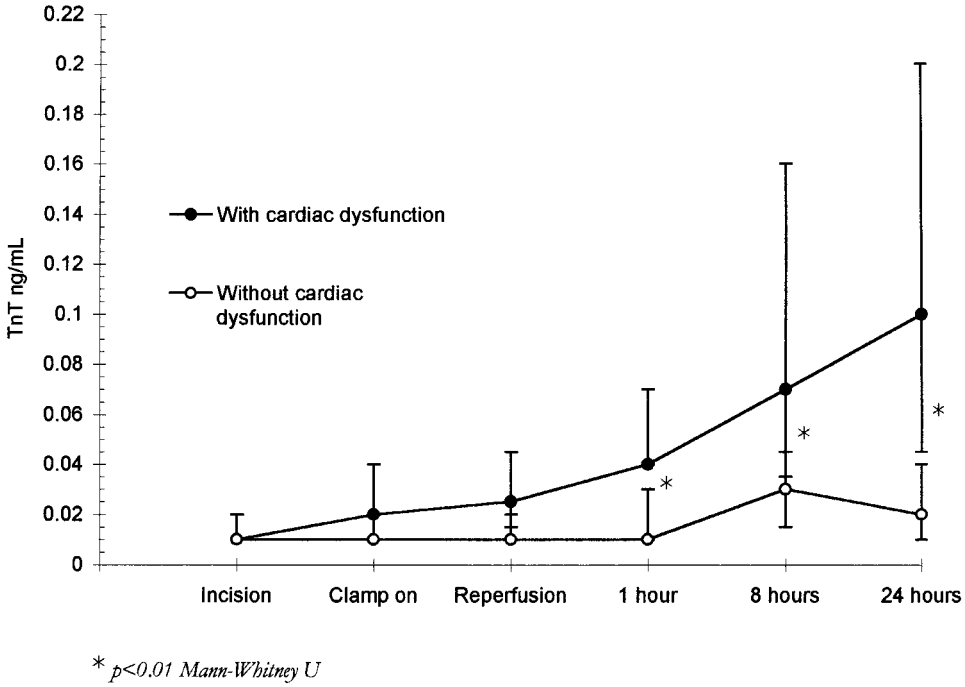

Fig 5. Median TnT levels are shown in eight patients who experienced cardiac dysfunction and in 17 patients who did not (two patients with TAAA with transmural MI were excluded).

correlation existed between peak TnT levels and minimum TPAS levels (r = –0.5; *P* = .01) and with peak LHP levels (r = 0.78; *P* = .001).

DISCUSSION

In this study, we demonstrated that supraceliac aortic crossclamping during surgery for TAAAs is associated with significant elevation of the myocardium injury marker TnT. TnT level changes in the 17 patients with AAA with infrarenal aortic crossclamping were minimal and nonsignificant, thus supporting the clinical observation that this type of surgery does not carry the same risk of myocardial injury. Furthermore, patients with TAAA who after the operation went on to experience signs of myocardial dysfunction had significantly higher levels of TnT than those patients who did not experience myocardial dysfunction.

This observation is similar to that reported by Lee et al[20] in patients who underwent noncardiac surgery. They found that a postoperative rise in TnT levels correlates significantly with the development of postoperative non-MI cardiac complications. Although the rise in TnT level in our patients with supraceliac aortic crossclamping was significant (even in those who experienced postoperative cardiac dysfunction), levels remained less than those seen in patients with transmural MI.[21-23]

Although it is not possible to exclude myocardial cell death as the cause of raised TnT levels in our patients with TAAA without histologic examination, a growing body of evidence now supports the existence of a clinical entity of cardiac injury that is associated with an intermediate rise in TnT levels in the absence of transmural MI or ischemic electrocardiographic changes. This entity comprises patients with angina, microinfarcts, and myocardial ischemia-reperfusion injury.[24-30] In this group of patients, the moderate rise in TnT level is due to cell-wall damage with subsequent release of the unbound cytosolic TnT.[31] Although the risk of subsequent MI and death is estimated to be 10.5% in patients with angina and an intermediate rise in TnT level (0.06-0.18 ng / mL),[32] such risks in noncardiac surgical patients with a similar rise in TnT level remain unknown. Yeager et al[33] attempted to quantify such risks by following up 8 vascular surgical patients with biochemical MI, as detected by creatine kinase-MB. Although they showed no significant long-term effects in this group, they agreed that their numbers were too small to produce any firm conclusions.

In our group of patients with TAAA with cardiac complications, myocardial dysfunction occurred during or a few hours after surgery, and the associated increase in TnT level was observed as early as 1 hour after reperfusion. Because the presence of significant myocardial ischemia or significant organ impairment between patients with TAAA who experienced cardiac dysfunction and those who did not was excluded before the operation, it is unlikely that the myocardial injury in these patients was due to primary myocardial ischemia. This assumption is also supported by the fact that the magnitude of TnT level changes in the two patients with MI was 10 times more than that seen in the cardiac dysfunction group. It is therefore likely that other factors such as mechanical stresses and remote ischemia-reperfusion injury during and after surgery have contributed to the cardiac injury observed.

In patients with supraceliac clamping and in the few minutes before aortic clamping, vasodilator drugs such as sodium nitroprusside and glyceryl trinitrate are given to achieve a controlled drop in peripheral vascular resistance and cardiac output in the anticipation of the sudden rise in peripheral resistance on aortic crossclamping. Immediately after declamping, the drop in peripheral vascular resistance and blood pressure may be severe and prolonged, thus requiring an infusion of inotropes such as adrenaline and noradrenaline to improve cardiac contractility and to increase peripheral resistance.

Although these mechanical and pharmacologic stresses to the cardiovascular system may correlate with the development of postoperative MI as previously shown by Hollier et al,[2] the correlation between these changes and the development of postoperative cardiac dysfunction has not been previously studied. In this study, we were unable to demonstrate a correlation between blood pressure changes and TnT level. We believe that this may be because the changes in blood pressure alone, as suggested by Hollier et al, may not adequately reflect the severity of mechanical stresses in these patients. However, correlating between cardiac output, peripheral vascular resistance, and the development of postoperative cardiac dysfunction may be a more accurate method.

The other possible explanation of the myocardial injury in these patients is remote ischemia-reperfusion injury after aortic declamping. If powerful enough, the burst of ODFR after reperfusion may overwhelm the natural antioxidant defenses and initiate a cascade of events that lead to proinflammatory cytokine production with local or remote cell injury and death.[10,34]

Unlike patients with AAA, patients with TAAA sustained a more severe oxidative stress and free rad-

ical injury, mainly because of splanchnic ischemia-reperfusion. This is shown by the more significant changes to LHP level immediately after splanchnic reperfusion. Although LHP and TPAS levels correlated significantly with ischemia time, TnT levels did not. This lack of correlation indicates that myocardial injury in these patients is not a function of absolute ischemia time but rather the ability of the antioxidant defensive mechanisms to cope with this ischemia. In an animal model, Horton and White[35-37] demonstrated that intestinal ischemia even for a brief period followed by reperfusion can lead to prolonged and significant cardiac contractile dysfunction and to significant LHP of cardiac cell membranes. They attributed these changes to oxygen free radial generation by intestinal xanthine oxidase. Ischemia-reperfusion of splanchnic organs other than the intestine can also lead to cardiac injury. Pretto[38] demonstrated that isolated hepatic ischemia-reperfusion can lead to a direct increase in coronary resistance and a drop in coronary blood flow and heart rate. The combined effect of intestinal and hepatic ischemia-reperfusion during TAAA surgery may therefore lead to myocardial cell damage. It remains difficult to ascertain a causal relationship between the higher incidence of major complications in patients with TAAA with myocardial dysfunction and the myocardial damage in these patients. It is more likely that the two are the result of a more global ischemia-reperfusion injury.

In summary, our data suggest that clamping of the aorta above the celiac vessels and without bypass grafting is associated with myocardial injury. This injury correlates with the severity of oxidative stress and with poor outcome. Patients undergoing AAA surgery are less likely to sustain such stresses and subsequently showed no evidence of myocardial damage during the operation. Measures to attenuate splanchnic ischemia and possibly oxidative stresses (such as the use of selective mesenteric shunting[39] and antioxidant augmentation) may therefore have a cardioprotective effect in patients with TAAA. Although mechanical stresses during this type of surgery may contribute to the sustained myocardial injury, these stresses remain invariably inevitable because of the nature of aortic surgery itself.

REFERENCES

1. Gilling-Smith GL, Worswick L, Knight PF, Wolfe JHN, Mansfield AO. Surgical repair of thoracoabdominal aortic aneurysm: 10 years experience. Br J Surg 1995;82;624-9.
2. Hollier LH, Symmonds JB, Pairolero PC, Cherry KJ, Hallet JW, Gloviczki P. Thoracoabdominal aortic aneurysm repair: analysis of postoperative morbidity. Arch Surg 1988;123:871-5.
3. Cox GS, O'Hara PJ, Hertzer NR, Piedmonte MR, Krajewski LP, Beven EG. Thoracoabdominal aneurysm repair: a representative experience. J Vasc Surg 1992;15:780-8.
4. Svensson LG, Crawford ES, Hess KR, Coselli JS, Safi HJ. Experience with 1509 patients undergoing thoracoabdominal aortic operations. J Vasc Surg 1993;17:357-70.
5. Charlson M, Peterson J, Szatrowski TP, MacKenzie R, Gold J. Long-term prognosis after peri-operative cardiac complications. J Clin Epidemiol 1994;47:1389-400.
6. Granger DN, Rutili G, McCord JM. Superoxide radicals in feline intestinal ischemia. Gastroenterology 1981;81:22-9.
7. Halliwell B. Reactive oxygen species in living systems: source, biochemistry, and role in human disease. Am J Med 1991;91(suppl):14S-22S.
8. Leff JA, Parsons PE, Day CE, et al Serum antioxidants as predictors of adult respiratory distress syndrome in patients with sepsis. Lancet 1993;341:777-80.
9. Halliwell B, Gutteridge JMC. Role of free radicals and catalytic metal ions in human disease: an overview. Methods Enzymol 1990;186:1-85.
10. Freeman BA, Crapo JD. Biology of disease, free radicals and tissue injury. Lab Invest 1982;47:412-26.
11. Mair J, Dienstl F, Puschendorf B. Cardiac troponin T in the diagnosis of myocardial injury. Crit Rev Clin Lab Sci 1992;29:31-57.
12. Muller Bardorff M, Freitag H, Scheffold T, Remppis A, Kubler W, Katus HA. Development and characterization of a rapid assay for bedside determinations of cardiac troponin T. Circulation 1995;92:2869-75.
13. Crawford ES, Snyder DM, Cho GC, Roehm JOF. Progress in the treatment of thoracoabdominal and abdominal aortic aneurysms involving celiac, superior mesenteric, and renal arteries. Ann Surg 1978;188:404-22.
14. Sawada SG, Segar DS, Ryan T, et al. Echocardiographic detection of coronary artery disease during dobutamine infusion. Circulation 1991;83:1605-14.
15. Bourdillon PD, Broderick TM, Sawada SG, et al. Regional wall motion index for infarct and non-infarct regions after reperfusion in acute myocardial infarction: comparison with global wall motion index. J Am Soc Echocardiogr 1989;2:398-407.
16. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med 1985;13:818-29.
17. Rice-Evans C, Nicholas-Miller J. Total antioxidant status in plasma and body fluids. Methods Enzymol 1994;234:279-93.
18. Nourooz-Zadeh J, Tajaddini-Sarmadi J, Wolff SP. Measurement of plasma hydroperoxide concentrations by the ferrous oxidation-xylenol orange assay in conjunction with triphenylphosphine. Ann Biochem 1994;220:403-9.
19. Katus HA, Rempis A, Neuman FJ, et al. Diagnostic efficiency of troponin-T measurement in acute myocardial infarction. Circulation 1991;83:902-12.
20. Lee TH, Thomas EJ, Ludwig LE, et al. Troponin-T as a marker for myocardial ischemia in patients undergoing major non-cardiac surgery. Am J Cardiol 1996;77:1031-6.
21. Abe S, Arima S, Yamashita T, et al. Early assessment of reperfusion therapy using cardiac troponin T. J Am Coll Cardiol 1994;23:1382-9.
22. Collinson PO, Moseley D, Stubbs PJ, Carter GD. Troponin T for the differential diagnosis of ischemic myocardial damage. Ann Clin Biochem 1993;30:11-6.
23. Alonsozana GL, Christenson RH. The case for cardiac troponin T: marker for effective risk stratification of patients with acute cardiac ischemia. Clin Chem 1996;42:803-8.

24. Hake U, Schmid FX, Iversen S, et al. Troponin-T, a reliable marker of perioperative myocardial infarction? Eur J Cardiothorac Surg 1993;7:628-33.
25. Gerhardt W, Ljungdahl L, Herbert AK. Troponin-T and CK MB (mass) in early diagnosis of ischemic myocardial injury: the Helsingborg Study 1992. Clin Biochem 1993;26:231-40.
26. Collinson PO, Moseley D, Stubbs PJ, Carter GD. Troponin T for the differential diagnosis of ischemic myocardial damage. Ann Clin Biochem 1993;30:11-6.
27. Stubbs P, Collinson P, Moseley D, Greenwood T, Noble M. Prospective study of the role of cardiac troponin T in patients admitted with unstable angina. Br Med J 1996;313:262-4.
28. Ravkilde J, Nissen H, Mickley H, Andersen PE, Thayssen P, Horder M. Cardiac troponin T and CK-MB mass release after visually successful percutaneous transluminal coronary angioplasty in stable angina pectoris. Am Heart J 1994;127:13-20.
29. Machler H, Gombotz H, Sabin K, Metzler H. Troponin T as a marker of perioperative myocardial cell damage. Adv Pharmacol 1994;31:63-73.
30. Mair P, Mair J, Koller J, Wieser C, Talasz H, Puschendorf B. Cardiac troponin T release in multiply injured patients. Injury 1995;26:439-43.
31. Katus HA, Remppis A, Scheffold T, Diederich KW, Kuebler W. Intracellular compartmentation of cardiac troponin T and its release kinetics in patients with reperfused and nonreperfused myocardial infarction. Am J Cardiol 1991;67:1360-7.
32. Lindahl B, Venge P, Wallentin L. Relation between troponin T and the risk of subsequent cardiac events in unstable coronary artery disease: the FRISC study group. Circulation 1996;93:1651-7.
33. Yeager RA, Moneta GL, Edwards JM, Taylor LM Jr, McConnell DB, Porter JM. Late survival after perioperative myocardial infarction complicating vascular surgery. J Vasc Surg 1994;20,4:598-606.
34. Bast A, Haenen GR, Doelman CA. Oxidants and antioxidants: state of the art. Am J Med September 1991;91 (suppl):2s-13s.
35. Horton JW, White DJ. Cardiac contractile injury after intestinal ischemia-reperfusion. Am J Physiol 1991;261(Heart Circ Physiol):H1164-70.
36. Horton JW, White DJ. Lipid peroxidation contributes to cardiac deficits after ischemia and reperfusion of the small bowel. Am J Physiol 1993;264(suppl):H1686-92.
37. Horton JW, White DJ. Free radical scavengers prevent intestinal ischemia-reperfusion mediated cardiac dysfunction. J Surg Res 1993;55:282-9
38. Pretto EA. Cardiac function after hepatic ischemia-anoxia and reperfusion injury: a new experimental model. Crit Care Med 1991;19:1188-94.
39. Cambria RP, Davison JK, Giglia JS, Gertler JP. Mesenteric shunting decreases visceral ischemia during thoracoabdominal aneurysm repair. J Vasc Surg 1998;27:745-74.

Submitted Apr 7, 1999; accepted Jul 15, 1999.

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