

SCA 11

RENAL DYSFUNCTION AND APROTININ IN ADULTS UNDERGOING THORACIC AORTIC SURGERY REQUIRING DEEP HYPOTHERMIC CIRCULATORY ARREST

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Introduction: Deep hypothermic circulatory arrest (DHCA) in adults undergoing thoracic aortic surgery with aprotinin has been associated with postoperative renal dysfunction^{1,2,3}. Initial trials with aprotinin in DHCA had demonstrated increased mortality and renal thrombi on autopsy; in retrospect, these events were probably due to inadequate anticoagulation³. A recent 9-yr retrospective review of DHCA with adequate heparinization identified five risk factors predicting renal dysfunction: the absence of dopamine, ≤ 800 ml of OR urine, ≥ 5 PRBC units transfused in the OR, hematocrit $\leq 21\%$, and ≤ 2100 ml of ICU urine (24 hr)¹. Two literature standards of renal dysfunction exist: a $\geq 50\%$ increase in baseline serum creatinine² and a $\geq 25\%$ decrease in creatinine clearance¹, as measured by the Cockcroft and Gault formula⁴. We reviewed our large contemporary DHCA experience to assess renal dysfunction and its correlation with antifibrinolytic exposure.

Methods: With IRB approval, 110 patient charts from 2000 and 2001 were retrospectively analyzed in a Microsoft Access database. Patients received either aprotinin or epsilon-aminocaproic acid (E-ACA). Aprotinin dosage was at either full Hammersmith (FH) dose (2 X 10⁶ kallikrein inhibition units (KIU) patient load, 2 X 10⁶ KIU bypass load, 5 X 10⁵ KIU/hr infusion) or half Hammersmith (HH) dose (1 X 10⁶ KIU patient load, 1 X 10⁶ KIU bypass load, 5 X 10⁵ KIU/hr infusion). E-ACA dosage was at either 5 g or 10 g initial load with 1g/hr IV infusion. Preoperative, intraoperative, and postoperative variables were examined. The computer software *Stata* was used for statistical analysis.

Results: Out of 110 patients, 76 (69.1%: 72 FH and 4 HH) were given aprotinin and 34 (30.9%) were given E-ACA. The following were not significantly different between antifibrinolytic groups: gender, age, BSA, CBC, PT/PTT, baseline creatinine, CPB time, DHCA time, ACT, heparin dose and protamine dose. However, 87.1% (27/31) of emergency cases, 88.2% (15/17) of reoperation cases, and 100% (26/26) of acute type A dissections received aprotinin (p=0.0007, p=0.0518, and p<0.00005 respectively). The renal outcomes are presented in Table 1.

Discussion: Severe renal dysfunction requiring dialysis is rare. This cohort size is underpowered to test for correlation with antifibrinolytic. The incidence of renal dysfunction is high but varies by 9.1% depending on definition. The total incidence of renal dysfunction after DHCA is similar to the recent 9-yr retrospective review (38%)¹. Renal dysfunction by either literature standard is clinically important because it correlated with increased length of stay in the ICU (p=0.014). The five risk factors for renal dysfunction after DHCA were not predictive in our cohort¹. Our own multivariate cohort analysis identified three predictive risk factors: age, DHCA time, and baseline serum creatinine. These three risk factors are similar to renal risk factors after CABG (age, baseline serum creatinine, CPB time)⁵. Aprotinin appears associated with an increased renal risk after DHCA. However, this significance depends on definition (p=0.006 vs. p=0.117). There is also major selection bias in the aprotinin group that may significantly affect renal risk (emergency, reoperation, and acute type A dissection). This high-risk patient cohort is likely confounding the renal effects due to aprotinin. A complete multivariate analysis is currently underway to assess the relative significance of these confounders.

References: [1] Mora Mangano CT, Neville MJ, Hsu PH, et al: Aprotinin, Blood Loss, and Renal Dysfunction in Deep Hypothermic Circulatory Arrest. *Circulation*. 2001;104:I276-I281. [2] Ehrlich M, Grabenwoger M, Cartes-Zumelzu, F et al: Operations on the Thoracic Aorta and Hypothermic Circulatory Arrest: Is Aprotinin Safe? *J Thorac Cardiovasc Surg*. 1998;115:220-5. [3] Smith CR, Spanier TB: Aprotinin in Deep Hypothermic Circulatory Arrest. *Ann Thorac Surg* 1999;68:278-86.[4] Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976;16:31-41.[5] Mora Mangano CT, Diamondstone LS, Ramsay JG, et al: Renal Dysfunction after Myocardial Revascularization: Risk Factors, Adverse Outcomes, and Hospital Resource Utilization. *Ann Intern Med*. 1998;128:194-203.

Table 1 Renal Outcome after DHCA

Dysfunction	Total (N=110)	Aprotinin (N=76)	E-ACA (N=34)	p-value
Baseline creatinine (mg/dl)	1.19 1.13	1.25 1.33	1.06 0.469	>0.05
>50% increase in plasma creatinine (mg/dl)	43 (39.1%)	36 (32.7%)	7 (6.4%)	0.006
>25% reduction in creatinine clearance (ml/min)	53 (48.2%)	40 (36.4%)	13 (11.8%)	0.117
Either standard of dysfunction	57 (51.8%)	44 (40.0%)	13 (11.8%)	0.044
New Dialysis	2 (1.8%)	2 (1.8%)	0	-