Postoperative risk factors for delayed neurologic deficit after thoracic and thoracoabdominal aortic aneurysm repair: A case-control study

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Objective: **Delayed neurologic deficit after thoracoabdominal or thoracic aortic repair is an unusual complication. We previously examined the preoperative risk factors associated with immediate neurologic deficit to consider their relationship to delayed neurologic deficit. In the current study we wanted to determine whether postoperative events influence the likelihood of delayed neurologic deficit, independent of preoperative risk factors.**

Methods: **We studied postoperative hemodynamics and cerebrospinal fluid (CSF) drain function in patients who had delayed neurologic deficit (cases) and those who did not (controls). Our database contains data for 854 patients with descending thoracic and thoracoabdominal aortic aneurysm. Cases and controls were identified with a random number generator to select controls in an approximate 4:1 ratio. We identified 18 cases and 67 controls. Further data were obtained from medical records.**

Results: **We found no differences between the groups with regard to oxygen transport abnormalities, eg, pneumothorax, repeat intubation, cardiac arrest, atrial or ventricular dysrhythmia, or dialysis. Significant differences between the groups were present for CSF drain complications (eg, kinks, blood in CSF): 6 of 18 (33%) in the case group versus 3 of 67 (4.5%) in the control group ($P < .003$). Wide fluctuation in mean arterial pressure (MAP) was significant ($P < .02$), mainly because of very low MAP in the cases ($P < .006$). When odds ratio was adjusted for preoperative risk factors of extent II thoracoabdominal aortic aneurysm, acute aortic dissection, and chronic aortic dissection, MAP less than 60 mm Hg and CSF drain complications produced the highest odds of delayed neurologic deficit.**

Conclusion: **No single risk factor explained the onset of delayed deficit. Rather, a combination of factors, especially lowest MAP and drain complications, produced the highest odds of deficit. Vigilant optimization of hemodynamics and immediate correction of CSF drain malfunction may prevent development of delayed neurologic deficit. (J Vasc Surg 2003;37:750-4.)**

As we continue to analyze patient outcome after thoracoabdominal aortic repair, delayed neurologic deficit has emerged as a unique clinical entity. Although the relationship of neurologic deficit immediately after thoracoabdominal aortic repair to duration and severity of spinal cord ischemia is well known, the cause of delayed neurologic deficit, ie, paraplegia or paraparesis after a period of observed normal neurologic function, is less certain. In an earlier cohort study we focused on the possible etiologic similarities between immediate and delayed neurologic deficit. We identified the preoperative factors of renal insufficiency, acute dissection, and extent II thoracoabdominal aortic aneurysm as significant,[1] which, with the addition of aortic clamp time and rupture, have also been identified as risk factors for immediate neurologic deficit.[2,3]

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In the current study we examined postoperative events that may increase risk for delayed neurologic deficit independently of the preoperative risk factors identified in our previous study. Postoperative risk factors had not been described previously in a large series or evaluated in an appropriate control population.

We hypothesized that delayed neurologic deficit is observed in patients with "vulnerable" spinal cord after thoracoabdominal aortic repair, in whom additional postoperative ischemic insults will lead to worsening spinal cord ischemia. Postoperative events that have been observed in the onset of delayed neurologic deficit include systemic hypotension and any other event that may exacerbate spinal cord ischemia, eg, increased cerebrospinal fluid (CSF) pressure or decreased oxygen delivery.

Because delayed neurologic deficit occurs relatively rarely, we believed a case-control study would best elucidate the proposed risk factors and determine the relative odds of postoperative risk factors occurring in either patients with delayed neurologic deficit (cases) or patients without neurologic deficit (controls).

METHODS

Between February 1991 and May 2001, 854 patients underwent graft repair of the descending thoracic or thoracoabdominal aorta. Thirty-eight (4.5%) patients with immediate neurologic deficit and 26 (3.0%) patients who died

Table I. Patient Demographics

Variable	*Cases*	*Controls*	P
Age (y)	65	64	.64
Female (%)	41	40	1.0
TAAAII (%)	41	19	.10
Acute dissection (%)	18	2	.03
Chronic dissection (%)	47	18	.03
COPD (%)	6	40	.009
Renal dysfunction (%)	35	13	.07
Cerebrovascular disease (%)	18	10	.39
Emergency (%)	0	8	.58
Previous aneurysm repair	29	49	.18

TAAAII, Thoracoabdominal aortic aneurysm extent II, from distal to left subclavian artery to below renal arteries; *COPD*, chronic obstructive pulmonary disease.

during surgery or immediately thereafter were excluded from the study. Twenty-one patients had delayed neurologic deficit. The study followed a case-control design with an approximate 4:1 control to case subject sampling ratio. Cases were identified as patients who demonstrated intact neurologic function on awakening from anesthesia but later lost that function. Loss of function was defined as paraplegia or paraparesis, with a score less than 5 using Tarlov criteria: 0, no motion; 1, motion without gravity; 2, motion against gravity; 3, able to stand with assistance; 4, able to stand and walk with assistance; and 5, normal function.

Controls had also undergone descending thoracic or thoracoabdominal aortic repair but did not demonstrate any postoperative neurologic dysfunction. Because of the relative homogeneity of the patient population and the consequent possibility of overmatching, we did not use an active control matching strategy. Patients were identified from our main patient database with a computerized random number generator written in SAS software. The 4:1 ratio was approximate because five charts for 72 controls identified with the random number process could not be obtained. Table I lists the demographics of the patients in each group.

On the basis of our clinical experience with patients who sustained delayed deficits, we hypothesized that CSF drain function, blood pressure maintenance and stability, and oxygen transport would be related to risk for deficit. Our database lacked detailed information on postoperative day-by-day hemodynamic and CSF drain function, so we reviewed medical charts to collect these data. Because several types of CSF drain malfunction were identified, we created a true-false summary variable for CSF drain complication that was true if the drain was removed early (ie, earlier than the third postoperative day), if the catheter was kinked, or if the CSF was blood-tinged. The specific hypothetical postoperative risk factors were identified before chart review and were pursued equally in the charts of cases and controls. Variables evaluated are listed in Table II.

Part of the rationale for selecting the case-control design was the difficulty involved in reviewing more than 700 charts for the control patient information when a representative random sample could be used instead. Because of the potential for preoperative risk factors to interfere with interpretation of postoperative course events, we performed multiple logistic regression analysis to adjust for potentially confounding effects of the preoperative characteristics.

Data from chart reviews were entered into SAS software and merged with data from our existing database. Univariate analyses were conducted with contingency table methods for categorical variables and with *t* test or Wilcoxon rank-sum test for continuous variables. Multivariable analyses were conducted with unconditional logistic regression. All computations were performed with SAS version 8.02 running under Windows 2000.

RESULTS

Eighteen cases had sufficient data for analysis and were compared with 67 randomly selected controls that met study criteria. Comparisons of postoperative risk factors are shown in Table II. In univariate analysis, cases relative to controls had a greater than 10-fold increase in odds of CSF drain complication. Patients with delayed neurologic deficit had increased odds of low mean arterial blood pressure (MAP). A wide fluctuation in MAP (as an index of blood pressure instability) was also a significant univariate risk factor with a greater prevalence in cases. On the other hand, atrial dysrhythmia and postoperative dialysis had nearly identical prevalence in both cases and controls.

Adjusted analysis is shown in Table III. Multiple logistic regression identified CSF drain complication and lowest MAP as significant independent risk factors. These estimates were adjusted for aneurysm extent, acute aortic dissection, and chronic aortic dissection. The adjusted odds ratios for CSF drain complication and low MAP (<60 mm Hg) were nearly double those seen in the univariate data (Table II). This indicates that confounding by the preoperative risk factors would have tended to reduce the size of the postoperative effects. Adjusted analysis showed that the associations between postoperative course factors and outcome were stronger than in the univariate case. The combination of low MAP and CSF drain complications produced the highest odds of deficit (Figure).

DISCUSSION

Delayed neurologic deficit, defined as paraplegia or paraparesis, occurs after a period of normal neurologic evaluation after thoracoabdominal aortic repair. The first case was reported in 1988, when deficit correction was thought to be beyond the surgeon's control.[4] A prospective randomized trial conducted by the same group failed to show any benefit in intraoperative CSF drainage.[5] This failure may have been due to study restrictions imposed by the institutional review board that limited CSF drainage to 50 mL. However, since then animal and clinical studies have confirmed that CSF drainage reduces CSF pressure and may improve spinal cord perfusion during aortic cross clamping.[6-11] More recently, two anecdotal reports in the literature showed reversal of delayed paraplegia with spinal

Table II. Postoperative risk factors for delayed neurologic deficit

	Cases (N = 18)		*Controls (N = 67)*				
Variable	*n*	*%*	*n*	*%*	*OR*	*95% CI*	P
Lowest HGB							.008+
5.5-8.6	11	61.1	15	22.4	5.45	1.80-16.50	
8.7-9.4	3	16.7	16	23.8	0.64	0.16-2.48	
9.5-10.8	3	16.7	18	26.9	0.54	0.14-2.10	
10.9-13.7	1	5.6	18	26.9	0.16	0.12-1.29	
Lowest MAP							.0006+
41-63	11	61.1	13	19.4	6.52	2.12-20.10	
64-71	4	22.2	17	25.3	0.84	0.24-2.90	
72-78	3	16.7	18	26.9	0.54	0.14-2.10	
79-100	0	0.0	19	28.3	0.07	0.01-1.17	
Highest-lowest MAP							.003+
13-33	2	11.1	18	26.9	0.34	0.07-1.63	
34-43	3	16.7	17	25.3	0.59	0.15-2.28	
44-53	4	22.2	19	28.3	0.72	0.21-2.47	
54-82	9	50.0	13	19.4	4.16	1.38-12.54	
CSF drain Complication	6	33.3	3	4.4	10.7	2.34-48.61	.003
Otherwise	12	66.7	64	95.6	1		
Atrial dysrhythmia	7	38.9	28	41.8	0.89	0.31-2.57	1.0
Otherwise	11	61.1	39	58.2	1		
Dialysis	1	5.6	6	9.0	0.60	0.07-5.32	1.0
Otherwise	17	94.4	61	91.0	1		

Lowest HGB, Lowest postoperative hemoglobin (in g/dL); lowest MAP, lowest postoperative mean arterial blood pressure (mm Hg); highest-lowest MAP, highest postoperative MAP, lowest postoperative MAP (an index of blood pressure instability); CSF drain complication, early removal, kink, nonfunction, hematoma, blood-tinged fluid; *OR*, common stratum-specific odds ratio; *P*, Fisher exact *P* value computed from contingency table, unless labeled with +, which indicates logistic regression maximum-likelihood *P* value against continuous variable.

Table III. Adjusted analysis

Variable	*Coefficient*	*OR**	*95% CI*	P
Lowest MAP <60	2.37	10.73	2.17-53.13	.004
CSF Complication	2.97	19.50	2.94-129.21	.003

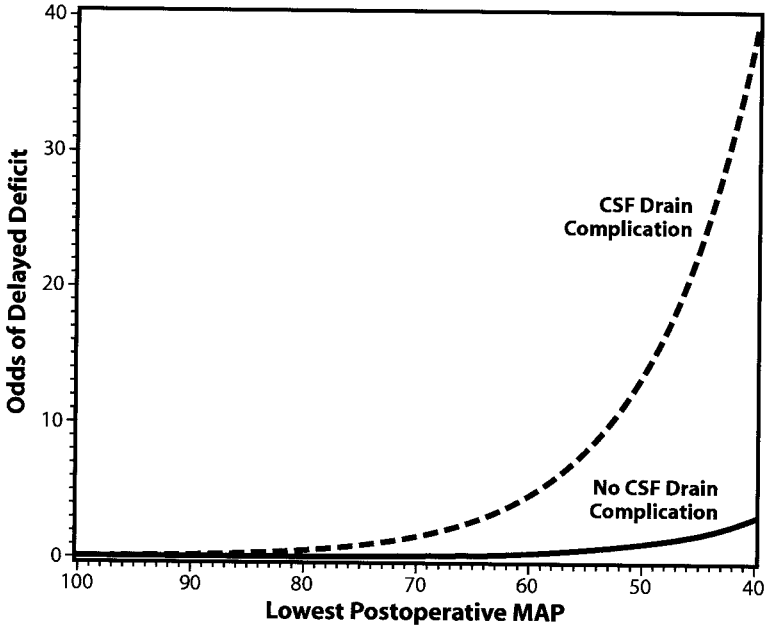
Lowest MAP < 60, lowest postoperative mean arterial pressure <60 mm Hg; CSF complication, nonfunction due to kink, clot, hematoma, blood-tinged fluid.

*Adjusted for preoperative risk factors extent II aneurysm, acute aortic dissection, chronic aortic dissection, and total aortic crossclamp time. Unconditional multiple logistic regression estimates.

cord decompression with CSF catheter drainage.[12,13] We subsequently reported a similar experience with 8 patients in whom delayed neurologic deficit developed.[14] Since then, multiple authors have reported significant improvement in patient neurologic function by using CSF drainage.[15-18] Currently we recommend CSF drainage by gravity intraoperatively and for 3 days postoperatively in all patients undergoing surgical repair involving the descending thoracic or thoracoabdominal aorta. We generally drain 10 to 15 mL of CSF hourly to maintain CSF pressure less than 10 mm Hg. Our anesthesiologist replaces the CSF drain immediately if it is bloody or not draining freely. Contraindications to inserting a CSF drain include active systemic infection, coagulopathy, and hemodynamic instability.

No single risk factor explains the onset of delayed deficit. Rather, a combination of factors produced the highest odds of deficit development. Although several potential risk factors have been identified, no studies have compared the occurrence of the risk factors in cases with their occurrence in an appropriate control group. Using multivariate analysis, we recently found that acute dissection, extent II thoracoabdominal aortic aneurysm, and renal insufficiency are independent preoperative predictors of delayed neurologic deficit.[1]

In multivariable analysis, only lowest postoperative MAP and CSF drain complications were significant predictors of delayed deficit. We retained dissection status and aneurysm extent (thoracoabdominal type II or otherwise) in the multivariable model so that the odds ratio estimates for MAP and CSF drain complications would be adjusted for the influence of these other factors. We also forced aortic cross-clamp time into the multivariable model so that the other estimates would be adjusted for it. Clamp time was not significant, and it did not change the conclusions regarding other factors. We were very much aware of the possibility of confounded postoperative results due to preoperative and intraoperative factors, and we accounted for this with the best epidemiologic tools available. The current study confirms the significance of postoperative risk factors, independent of preoperative risk factors. Based on the findings of this study, the odds of development of delayed neurologic deficit are significantly increased with MAP less than 60 mm Hg or CSF drain malfunction in the postoperative period. This indicates that hemodynamic instability and interference with CSF drainage have a major



Odds of delayed neurologic deficit by lowest postoperative mean arterial blood pressure *(MAP)* with or without CSF drain complication. Odds are referenced to 1. For example, a patient with MAP 40 mm Hg and a CSF drain complication would have 40:1 odds of delayed neurologic deficit.

role in development of delayed neurologic deficit, regardless of baseline risk factors. In univariate analysis, hemoglobin less than 8.6 g/L was also associated with delayed deficit, but lowest postoperative hemoglobin and lowest postoperative MAP were highly correlated, probably through blood loss or hemodilution from fluid resuscitation. Lowest MAP accounted for enough of the covariance between hemoglobin and delayed deficit for hemoglobin to be dropped from the final multivariable model.

The mechanism by which CSF drainage provides beneficial effects is not clearly understood. However, it is thought that because the spinal cord is housed in a bony spinal canal any small increase in spinal cord volume, eg, spinal cord edema, can produce a substantial rise in CSF pressure. The increased CSF pressure can lead to so-called compartment syndrome in the spinal column, similar to that seen with increased intracerebral edema or limb edema. CSF drainage may improve perfusion of the spinal cord by reducing CSF pressure, similar to the improvement in cerebral perfusion with ventriculostomy or in limb perfusion with fasciotomy.[8-13]

We speculate that delayed neurologic deficit after thoracoabdominal aortic repair may result from a "second hit" phenomenon. Although the adjuncts distal aortic perfusion and CSF drainage may protect the spinal cord intraoperatively and reduce the incidence of immediate neurologic deficit, the spinal cord remains vulnerable during the early postoperative period. Additional ischemic insult caused by hemodynamic instability and CSF drainage catheter malfunction may constitute a second hit, causing delayed neurologic deficit. Postoperatively, vigilance in monitoring and correcting hypotension and CSF drain problems may prevent additional ischemic injury to the spinal cord. Furthermore, early recognition of delayed neurologic deficit and prompt treatment with CSF drainage, as well as optimization of hemodynamic status, may help restore neurologic function.

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