Can particulate extraction from the ascending aorta reduce neurologic injury in cardiac surgery?

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Objective: This study examined whether extraction of particulate emboli using intra-aortic filtration could decrease neurologic outcomes.

Methods: Patients (N = 582) were enrolled in a prospective, controlled study and alternately assigned to the therapy arm (n = 304; intra-aortic filtration) or control arm (n = 278). Preoperative, procedural, and postoperative data were collected. Neurologic examinations included the National Institutes of Health Stroke Scale, Glasgow Coma Scale, and memory tests. Investigators administering neurologic tests were blinded to the study arm. By the use of logistic regression and propensity matching, composite neurologic outcomes (transient ischemic attack, stroke, delirium, coma, and memory deficit) were evaluated.

Results: Patients in the filter group experienced a lower incidence of adverse neurologic outcomes than patients in the control group (4.3% vs 11.9%) ($P < .001$). There were significantly less transient ischemic attacks (0% vs 1.4%), delirium (3.0% vs 6.5%), and memory deficit (1.3% vs 6.2%). There were fewer strokes in the filter group compared with the control group (0.7% vs 2.2%), although the sample size was too small for a significant finding. Both groups experienced 1 coma outcome. The use of a filter was associated with an adjusted odds ratio of 0.375, implying that a patient who does not receive a filter is 2.7 times more likely to experience an adverse neurologic event. Logistic modeling also demonstrated that there are increasing chances of poor neurologic outcome with increasing age. The model indicates that there may be an increasing protective benefit from the filter with increasing age, although the interaction was not significant.

Conclusions: The extraction of particulate emboli using intra-aortic filtration resulted in decreased neurologic outcomes.

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Intra-aortic filtration entered the cardiac surgeon's armamentarium in 1999. At present, it remains the only available method of capturing and extracting particulate emboli from the circulation. Since its introduction, numerous studies have been published highlighting risks to the patient undergoing cardiac surgery posed by particulate emboli and drawing links between aortic atherosclerosis, liberation of particulate debris during surgery, and injury to distal organs.[1-5]

Several studies have examined intra-aortic filtration and described its effects. In 2000, Reichenspurner and colleagues[6] reported that the extraction of particulate emboli in patients undergoing cardiac surgery was feasible using intra-aortic filtration. In a series of 77 patients, this article highlighted the capture and removal of fibrous atheroma and other particulate debris. A larger study by Harringer and the International Council of Emboli Management (ICEM)[7] showed that the filter extracted particulate material from 240 of 243 patients, and that 62% of the filters contained fibrous atheroma, which is of particular interest because the body does not lyse fibrous atheroma.

Whereas 2 studies established the filter's ability to capture and remove emboli, more recent studies examined the clinical relevance of emboli capture and removal. By using a published and validated stroke risk index, Schmitz and Blackstone[8] found that patients undergoing coronary artery bypass graft (CABG) receiving intra-aortic filtration experienced approximately half the expected number of severe neurologic outcomes. In high-risk patients undergoing combined CABG and intracardiac procedures, even greater benefit was found.[9] In these patients, Wimmer-Greinecker[9] reported 74% fewer type I outcomes (stroke, transient ischemic attack [TIA], coma, and death as the result of neurologic causes) when compared with a previous study.[10] The current investigation used a prospective, controlled study design to isolate the effect of the filter and examine whether the extraction of particulate emboli can reduce neurologic outcomes during cardiac surgery.

Methods

Eligible patients included all patients scheduled for CABG, valve, or combined CABG and valve procedures in our center between March 1999 and May 2002. Patients were excluded from the study if they presented with carotid stenosis greater than 70% or left ventricular ejection fraction less than 20% or if they received off-pump surgery. Because some of the neurologic assessments included verbal tests, patients who did not speak German as their mother tongue were also excluded. The study was approved by the local ethics committee and institutionally sanctioned; patient consent was obtained.

Preoperatively, patients were nonrandomly assigned to either the filter or control arm of the study at alternating intervals. Some flexibility in the time periods was used to keep enrollment numbers in both groups similar. Patients in both study arms received standard surgery per the normal protocols and procedures of our center. These procedures included cardiopulmonary bypass using aortic and 2-stage venous cannulas, a target flow rate of 2.4 L/m^2 · min, and a core body temperature of 32°C to 34°C. Myocardial protection was achieved using Buckberg's cold blood cardioplegia or Bretschneider's cardioplegia. Central anastomoses were sewn using a partial clamp after removal of the aortic crossclamp.

Patients in the filter arm received intra-aortic filtration in addition to their standard procedures. The intra-aortic filtration device consisted of a 120-micron heparin-coated polyester mesh placed in the aorta through a side port in the aortic cannula (EMBOL-X System, Edwards Lifesciences, Irvine, Calif). Filter placement occurred immediately before crossclamp release, and the device remained indwelling until the patient was weaned off bypass. Full details of the methods of filter usage have been previously described.[6-8] Filters were collected and sent to a central laboratory for analysis (Stanford University, Palo Alto, Calif).[7] Final enrollment included 304 patients in the filter group and 278 patients in the control group.

Neurologic assessment was performed on all patients at several points: preoperatively, 48 hours postoperatively, and at discharge (typically on the seventh postoperative day). Examinations included the National Institutes of Health Stroke Scale, Glasgow Coma Scale, and memory deficit questions. Neurologic examiners received identical training in the Neurology Department of Bonn University Hospital and were blinded to the study arm of each patient.

Neurologic end points for the composite outcome included stroke, TIA, coma, delirium, and memory deficit. Strokes were defined as a new focal neurologic deficit, confirmed by cranial computed tomography (CT) scan showing a new ischemic lesion. CT scans were ordered for patients with neurologic problems equivalent to an National Institutes of Health stroke score change of 4 or greater from baseline that did not resolve within 24 hours. Changes were defined as TIA if they substantially resolved in 24 hours and presented a negative CT scan. Coma applied to patients not regaining consciousness in the 24 hours after termination of sedation. Delirious patients exhibited confusion or an altered state of consciousness during hospitalization. Coma and delirium were also assessed clinically. The determination of memory loss used 5 questions regarding the patient's operation and hospital stay. Memory deficit in nondelirious patients was defined as clinical retrograde amnesia and assessed through postoperative questioning. Patients giving erroneous answers to 2 or more memory assessment questions were judged as memory deficient. Patients assessed with memory deficit or delirium at any time were categorized as memory deficit or delirium end points even if symptoms resolved by discharge.

Statistical Methodology

A statistical analysis investigated the effects of filter use on a composite neurologic outcome consisting of stroke, TIA, coma, delirium, or memory deficit. Each patient with at least 1 of these components was included as an adverse outcome. Because filters were not assigned in a prospective randomization scheme, a propensity score approach was taken to account for possible differences between treatment groups.[11] Of the 582 patients enrolled in this study, 46 experienced a qualifying composite event.

In all tables of univariable results, P values associated with continuous variables were generated by Wilcoxon 2-sample tests because the factors were not normally distributed. For the categoric variables, patient demographics between groups were compared using χ^2 tests or, if small expected cell frequencies, exact tests. Continuous variables are presented as means ± standard deviations, and categoric variables are presented as percentages.

Logistic regression modeling was used for both the propensity model and the model for composite outcome. Linearity assumptions for logistic models were checked, and appropriate data transformations were made. Lists of variables considered in the models are given in Appendix 1. The strategy for both models was to include only those factors that are known before procedure, including the type of procedure. Any variables with low frequency of occurrence were not used. Mean value imputation was used in the case of missing values for "missingness" of up to approximately 10%.

The strategy for obtaining a propensity model was to first develop a parsimonious model to describe patients who received filters. Stepwise selection techniques were used with a *P* value of .15 for entry. A *P* value of .10 was considered statistically significant. Model selection was validated using bootstrap techniques.[12] After the model was finalized, additional nonsignificant factors were included to adjust for other possible differences. Selected demographic, preoperative, and procedural variables for the matched population are shown in Appendix 2. This final nonparsimonious model produced a propensity score for each patient that predicts the probability of being a patient who received a filter.

To assess the quality of this score, patients were ranked by increasing propensity for filter and grouped accordingly into 5 subgroups or quintiles. If the propensity score has been constructed well, there should not be significant differences in baseline characteristics between patients in the filter and non-filter groups. In addition, the propensity score was used to match patients from the filter and non-filter groups.[13] In this way, a subset of the total population was obtained that behaved like a randomized group. The final model was verified on this subset.

Logistic modeling of the outcome variable included the filter group variable and then used stepwise selection techniques to determine other significant adjustments. A *P* value of .15 was used for entry and .10 was considered statistically significant. Model selection was validated using bootstrap techniques. After all baseline and procedural adjustments were made, the propensity score was added to the model.

Results

Demographic, preoperative, and procedural descriptors of the filter group are given in Tables 1 and 2. The logistic model for the filter group, used to construct a propensity score, is given in Table 3. The model presented has a reasonable fit but not good predictive ability (C statistic = 0.64). Patients who had a history of carotid stenosis or low cardiac output were more likely to get a filter. Patients with aortic disease, hypercholesterolemia, or history of congestive heart failure were less likely to receive a filter. Female patients were also less likely to receive a filter.

Quintiles for the filter group showed good matching across characteristics within each quintile as determined by *P*values of greater than .05, which indicate a lack of significant differences for the characteristics. One-to-one matching was performed between the groups using the propensity score. A total subpopulation of 474 patients was obtained; 39 of the 46 outcomes were retained in the subpopulation. Appendix 2 characterizes this group on the basis of the distinguishing characteristics for the filter group. The matching process has balanced the differences well.

Selected demographic, clinical history, and procedural descriptors for composite outcomes are shown in Table 4. A summary of individual composite measures is shown in Table 5. There was a significant difference between the filter and no-filter groups for TIA (*P* = .051), delirium (*P* = .044), and memory deficit (*P* = .002). The number of strokes was decreased in the filter group compared with the no-filter group (0.7% vs 2.2%), although the difference was not significant. Comparing the composite outcomes between the filter (13/304, 4.3%) and no-filter (33/278, 11.9%) groups showed significantly (*P* = .001) less neurologic outcomes in the patients with filters.

Table 6 presents the logistic model results for the entire population with the propensity score included (C statistic = 0.75). The use of a filter during cardiac surgery is associated with an adjusted odds ratio of 0.375. This implies that a patient who does not receive a filter is approximately 2.7 times as likely to experience an outcome after adjusting for other significant factors.

Increasing age is also predictive of poor outcome (Figure 1). Note that the variable in the model is log transformed. This implies the impact of increasing age with respect to outcome is not as great for younger patients. The effect is stronger for older patients. The benefit of the filter seems to increase with increasing age, although the interaction of age and filter use on composite outcome did not reach significance. A history of liver dysfunction (odds ratio = 3.111) and peripheral vascular disease (odds ratio = 2.288) increases the chances for a neurologic outcome. A history of myocardial infarction occurring greater than 7 days preoperatively (odds ratio = 0.493) is protective of outcome.

The propensity score is not significant in the model, nor did it alter the magnitude or direction of any of the findings. The model applied to the matched subset population agrees well with the results for the entire population (data not shown). All findings were in agreement with the exception of peripheral vascular disease (no longer significant). The results of these propensity score methods confirm the benefit of filter use after accounting for the lack of randomized treatment groups.

Particulate debris was extracted from 98% of patients receiving intra-aortic filtration. Greater than 72% of the filters contained fibrous atheroma, including grumous and fibrocalcific atheroma. Platelets and fibrin were found in 69% of filters, thrombus clot was found in 8%, and medial tissue was found in 1.3%.

Discussion

A flurry of activity and innovation in the field of cardiac surgery have been seen in the last 10 years. In the ongoing quest to reduce complications and trauma, progress has been made in minimally invasive tools and techniques. Beating heart surgery has received unprecedented attention, which has resulted in the development of sophisticated retractors, stabilizers, and heart positioners. Robotic surgery has rapidly evolved. Many have theorized that these advances should improve neurologic outcomes.

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TABLE 1. Patient demographics and clinical history by filter group

Parameter		No filter	Filter	*P* value
Total number of patients	N	278	304	
Patient age	N	277	304	.072
	Mean ± SD	66.7 ± 9.00	65.4 ± 9.31	
	Median	68.0	66.0	
Male gender	n/N (%)	198/276 (71.7)	239/304 (78.6)	.055
Endocarditis	n/N (%)	3/273 (1.1)	3/302 (1.0)	1.000
Carotid stenosis > 50%	n/N (%)	15/264 (5.7)	36/295 (12.2)	.008
Congestive heart failure	n/N (%)	15/274 (5.5)	9/301 (3.0)	.137
Preop LVEF	N	276	300	.155
	Mean ± SD	59.6 ± 13.74	58.1 ± 14.49	
	Median	63.0	60.0	
NYHA class	N	274	301	.107
1	n (%)	26 (9.5)	15 (5.0)	
2	n (%)	94 (34.3)	98 (32.6)	
3	n (%)	110 (40.1)	143 (47.5)	
4	n (%)	44 (16.1)	45 (15.0)	
Unstable angina	n/N (%)	43/276 (15.6)	49/299 (16.4)	.792
Aortic disease	n/N (%)	57/274 (20.8)	40/303 (13.2)	.015
Acute MI	n/N (%)	90/276 (32.6)	100/302 (33.1)	.898
MI (>7 d)	n/N (%)	109/275 (39.6)	135/299 (45.2)	.182
Left main disease	n/N (%)	62/274 (22.6)	81/299 (27.1)	.218
Atrial arrhythmia	n/N (%)	46/271 (17.0)	56/296 (18.9)	.547
Ventricular arrhythmia	n/N (%)	25/269 (9.3)	32/298 (10.7)	.568
Low cardiac output	n/N (%)	12/274 (4.4)	24/302 (7.9)	.077
Aortic plaque grade	N	230	269	.397
I	n (%)	139 (60.4)	163 (60.6)	
II	n (%)	65 (28.3)	66 (24.5)	
≥III	n (%)	26 (11.3)	40 (14.9)	
Transient ischemic attack	n/N (%)	32/276 (11.6)	38/299 (12.7)	.683
Stroke	n/N (%)	16/274 (5.8)	20/304 (6.6)	.713
Neurologic deficit	n/N (%)	7/276 (2.5)	6/300 (2.0)	.665
Diabetes (insulin-dependent)	n/N (%)	37/276 (13.4)	33/304 (10.9)	.346
Diabetes (oral medications)	n/N (%)	38/277 (13.7)	35/304 (11.5)	.423
Smoker	n/N (%)	58/213 (27.2)	72/205 (35.1)	.081
Alcohol use >3	n/N (%)	10/254 (3.9)	7/282 (2.5)	.337
Renal dysfunction	n/N (%)	31/275 (11.3)	43/303 (14.2)	.294
GI bleed	n/N (%)	20/268 (7.5)	23/298 (7.7)	.909
Obesity	n/N (%)	160/275 (58.2)	159/303 (52.5)	.168
Liver dysfunction	n/N (%)	30/264 (11.4)	27/292 (9.2)	.411
Peripheral vascular disease	n/N (%)	58/273 (21.2)	53/296 (17.9)	.315
Pulmonary dysfunction	n/N (%)	60/277 (21.7)	58/301 (19.3)	.476
Hypertension	n/N (%)	222/276 (80.4)	235/303 (77.6)	.397
Hypercholesterolemia	n/N (%)	222/276 (80.4)	220/303 (72.6)	.027

LVEF, Left ventricular ejection fraction; *MI,* myocardial infarction; *GI,* gastrointestinal; *NYHA,* New York Heart Association. *P* values: Wilcoxon 2-sample test, χ^2 test, and Fisher exact test.

Despite this intense effort, neurologic injury remains a devastating and tenacious surgical complication. Patients, families, surgeons, and the entire health care system bear a great burden each time a cardiac surgery ends in an adverse cerebral outcome. Roach and colleagues'[5] landmark article looked at 2108 patients across 24 centers and demonstrated that 6.1% of patients undergoing CABG experience an adverse cerebral outcome, a far more common phenomenon than previously recognized. They further reported that these patients demonstrated 5 to 10 times the mortality and 2 to 4 times the length of stay in intensive care, and required 3 to 6 times the prolonged care when compared with patients without adverse cerebral events. Although a multifactorial cause of this problem is recognized, aortic atheromatosis has repeatedly been reported as the greatest risk factor, and recent articles have highlighted the central role of particulate emboli in neurologic injury.[1,2,5]

Early studies using transesophageal echocardiography and transcranial Doppler demonstrated the embolic activity associated with surgical manipulation of the heart and the aorta during surgery.[3] In patients receiving intra-aortic filtration, the filter is deployed during the surgical period most

TABLE 2. Procedure category by filter group

Parameter		No filter	Filter	*P* value
Total number of patients	N	278	304	
Emergency surgery	n/N (%)	6/275 (2.2)	6/302 (2.0)	.870
Valve procedure	n/N (%)	20/278 (7.2)	11/304 (3.6)	.055
CABG	n/N (%)	226/278 (81.3)	258/304 (84.9)	.250
CABG/valve combination	n/N (%)	28/278 (10.1)	29/304 (9.5)	.829
Other procedure	n/N (%)	4/278 (1.4)	6/304 (2.0)	.754
Previous CABG or valve	n/N (%)	7/275 (2.5)	4/299 (1.3)	.292

CABG, Coronary artery bypass graft. *P* values: χ^2 and Fisher exact test.

TABLE 3. Adjusted logistic regression results (propensity model) for the filter group

Outcome	Coefficient	SE	Odds ratio	Odds ratio CI	*P* value
Filter (N = 582, No. filters = 304)					
Demographics:					
Patient age	−0.013	0.010	0.988	(0.969, 1.006)	.195
Female gender	−0.263	0.208	0.769	(0.511, 1.155)	.206
Clinical history:					
Carotid stenosis > 50%	0.960	0.331	2.611	(1.366, 4.992)	.004
Low cardiac output	1.034	0.435	2.812	(1.199, 6.595)	.017
Aortic disease	−0.633	0.264	0.531	(0.316, 0.891)	.017
Congestive heart failure	−1.011	0.517	0.364	(0.132, 1.002)	.050
Hypercholesterolemia	−0.553	0.208	0.575	(0.383, 0.865)	.008
Procedure:					
Valve procedure	−0.393	0.416	0.675	(0.298, 1.526)	.345
CABG/valve combination	0.097	0.339	1.102	(0.567, 2.142)	.774

CI, Confidence interval. Wald χ^2 statistics and *P* values; C statistic = 0.64; Hosmer-Lemeshow goodness of fit: χ^2 = 4.90, *df* = 8, *P* value = .77.

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associated with embolization, including partial clamping, sewing anastomoses, and removal of the aortic crossclamp. Intra-aortic filtration has emerged as the only technology to date capable of capturing and removing particulate emboli from the circulation. Previous reports by the ICEM Study Group focused analysis on a multicenter registry designed to gain statistical relevance by pooling data. These studies have been instrumental in demonstrating that intra-aortic filtration can be performed safely, that it successfully captures and removes particulate debris from the aorta, and that postoperative complications are reduced when compared with risk indices and historical controls.

Prior studies by the ICEM benefited from the ability to draw from 17 participating centers, allowing the aggregate patient group to reach more than 1600 patients in a consecutive enrollment registry. A study of this size has the advantage of providing meaningful background statistics, because category sizes remain large even when subgroups are examined. Because of this, important subset studies such as that reported by Schmitz and Blackstone[8] on behalf of the ICEM Study Group could look at a subset of patients undergoing only CABG in enough detail to assess their outcomes with a published, validated stroke risk index. They reported approximately 50% fewer neurologic outcomes in patients receiving intra-aortic filtration when compared with expected events (1.5% vs 3.4%, P = .03).

Similarly, there were enough patients for Wimmer-Greinecker[9] to examine a high-risk group of patients receiving concomitant CABG and intracardiac surgery. In his presentation at the 2001 European Association for Cardiothoracic Surgery meeting in Lisbon, Wimmer-Greinecker reported 74% fewer type I neurologic outcomes in this group when compared with a previous study.

This is the first study comparing a control group with a filter group in a single center. Although the study loses the power of the aggregate numbers, it gains the advantage of greater homogeneity through greater control over the procedural variables and patient population. All patients underwent operations by the same surgeons, at the same center, with the same tools and techniques. The procedure mix was very similar. The same outcome definitions and assessments were applied to all patients across both arms. The effect of the intra-aortic filter is thus more isolated than in previous investigations.

Exclusion criteria were applied in a further effort to ensure homogeneity across study arms. Patients with carotid stenosis greater than 70% were excluded because of the possibility of carotid effects on neurologic outcome con-

TABLE 4. Selected demographics, clinical history, and procedure category by composite outcome

Parameter	Statistic	No outcome	Yes outcome	*P* value
Total number of patients	N	536	46	
Demographics:				
Patient age	N	535	46	.016
	Mean ± SD	65.7 ± 9.27	69.3 ± 7.32	
	Median	67.0	70.5	
Male gender	n/N (%)	405/534 (75.8)	32/46 (69.6)	.343
Clinical history:				
Congestive heart failure	n/N (%)	21/529 (4.0)	3/46 (6.5)	.429
Carotid stenosis >50%	n/N (%)	45/515 (8.7)	6/44 (13.6)	.274
Calcification ascending aorta	n/N (%)	188/522 (36.0)	19/46 (41.3)	.475
Aortic disease	n/N (%)	85/531 (16.0)	12/46 (26.1)	.079
MI (>7 d)	n/N (%)	178/532 (33.5)	12/46 (26.2)	.019
Atrial arrhythmia	n/N (%)	88/522 (16.9)	14/45 (31.1)	.017
Transient ischemic attack	n/N (%)	60/529 (11.3)	10/46 (21.7)	.039
Smoker	n/N (%)	118/383 (30.8)	12/35 (34.3)	.671
Renal dysfunction	n/N (%)	66/532 (12.4)	8/46 (17.4)	.332
Liver dysfunction	n/N (%)	47/513 (9.2)	10/43 (23.3)	.008
Peripheral vascular disease	n/N (%)	96/523 (18.4)	15/46 (32.6)	.019
Pulmonary dysfunction	n/N (%)	103/532 (19.4)	15/46 (32.6)	.032
Hypertension	n/N (%)	419/533 (78.6)	38/46 (82.6)	.524
Procedure:				
Emergency surgery	n/N (%)	10/531 (1.9)	2/46 (4.3)	.247
Valve procedure	n/N (%)	29/536 (5.4)	2/46 (4.3)	1.000
CABG	n/N (%)	449/536 (83.8)	35/46 (76.1)	.182
CABG/valve combination	n/N (%)	48/536 (9.0)	9/46 (19.6)	.034
Previous CABG or valve	n/N (%)	9/530 (1.7)	2/44 (4.5)	.203
Treatment:				
Filter	n/N (%)	291/536	13/46	.001

P values: Wilcoxon 2-sample test, χ^2, and Fisher exact test.

TABLE 5. Summary of composite neurologic outcomes

Parameter		No filter	Filter	*P* value
Total number of patients	N	278	304	
Stroke	n/N (%)	6/278 (2.2)	2/304 (0.7)	.161
Transient ischemic attack	n/N (%)	4/278 (1.4)	0/304 (0.0)	.051
Delirium	n/N (%)	18/278 (6.5)	9/304 (3.0)	.044
Coma	n/N (%)	1/277 (0.4)	1/304 (0.3)	1.000
Memory deficit	n/N (%)	17/276 (6.2)	4/304 (1.3)	.002
All composite outcomes	n/N (%)	33/278 (11.9)	13/304 (4.3)	.001

P values: χ^2 and Fisher exact test.

founding the effects of the surgery. In addition, patients with less than 20% left ventricular ejection fraction were also excluded. These patients were excluded to ensure that all patients could be assessed with the complete range of neuropsychologic tests that were part of the full protocol.

Of the 46 composite neurologic outcomes, the filter group had 28.3% (13/46) and the control group had 71.7% (33/46). As expected, individual subcategories of neurologic injury had less statistical power, although TIA (P = .05), delirium (P = .04), and memory deficit (P = .002) each achieved significance independently. The stroke subcategory trended toward reduced occurrence in the filter group. In parallel with the overall reduction of individual outcomes, fewer patients experienced a composite adverse neurologic outcome in the filter group (13/304, 4.3%) when compared with the control group (33/278, 11.9%) (P = .001). That some preoperative variables provided a protective benefit or were predictive of an outcome may be caused in part by the low incidence of outcomes in this population or other possible coexisting conditions.

Preoperative variables between the 2 groups showed some differences, but these were adjusted for in the logistic model. Variables with significant influence and sufficient frequency were included in the propensity score model.

TABLE 6. Logistic regression model results with propensity score included for composite neurologic outcome

Outcome	Coefficient	SE	Odds ratio	Odds ratio CI	*P* value
Composite outcome					
(N = 582, no. events = 46)					
Demographics					
Patient age (log transformed)	2.762	1.387	15.83	(1.044, 240.0)	.047
Clinical history					
Liver dysfunction	1.135	0.410	3.111	(1.393, 6.949)	.006
Peripheral vascular disease	0.828	0.354	2.288	(1.143, 4.578)	.019
MI (>7 d)	−0.706	0.362	0.493	(0.243, 1.002)	.051
Procedure:					
Filter used	−0.980	0.355	0.375	(0.187, 0.752)	.006
Probability of filter (propensity score adjustment)	−0.260	1.349	0.771	(0.055, 10.85)	.847

Wald χ^2 statistics and *P* values; C statistic = 0.75; Hosmer-Lemeshow goodness of fit: $\chi^2 = 7.29$, $df = 8$, *P* value = .50.

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That some patients were more likely to receive a filter or not with the presence of certain preoperative variables was probably because a formal randomization scheme was not applied during patient selection. The propensity score was included in the model of outcome as an adjustment to compensate for bias. Although the propensity matching is a multivariate method that is the observational analog of randomization and controls for observed variables, it does not control for unobserved variables. Nonetheless, this model considered 37 variables and used all significant variables (n = 9) that provided good matching ($P > .05$ for variables) using a large percentage of the population. The model results remained consistent within the matched subset.

Important findings in this study include the benefit of filter use and the detriment of increasing age. Many studies have identified older patient age as a significant risk for adverse neurologic outcomes. The reason for this may in part be caused by increased preoperative risk conditions. The current results indicate that an 80-year-old patient with the filter might expect the equivalent outcome of a 55-year-old without the filter. Although the interaction of age and filter on outcomes was not significant, probably because of the low incidence of outcomes, there is a trend in this direction that warrants further investigation. It seems the older population may greatly benefit from intra-aortic filtration.

The mechanism for these results is most likely the extraction of particulate emboli from the aorta before they can travel distally and occlude important blood vessels. The chain of events—aortic atheroma, surgical manipulation, embolization, distal travel, and arterial occlusion—is apparently impeded when the emboli are captured and removed, making arterial occlusion less likely.

Two approaches have now been used to examine intra-aortic filtration. Previous ICEM studies have demonstrated the breadth of applicability of the filter in extracting particulate emboli safely in many patients. In addition, these studies have strongly suggested a clinical benefit. In our single-center controlled study, the evidence for a clinical benefit from filtration has become even more compelling. An even stronger study would combine breadth with control in a multicenter, randomized, controlled study.

Limitations

Further study could improve on the present investigation in several ways. A larger sample size could help to determine the effect of intra-aortic filtration on individual neurologic outcome categories. Our finding was notably most significant with the composite of neurologic outcomes. Although we believe that intra-aortic filtration has a significant effect on focal neurologic events such as stroke and coma, enrollment in the present study is not high enough to show more than a trend in these areas. Furthermore, some of the individual outcomes are likely to be correlated. To address this possibility, we have only included patient outcome results in which each patient is counted only as demonstrating 1 of the 5 neurologic measures or not. The outcome of composite neurologic finding represented less than 10% of the population of 582 patients.

A model built on 46 events must be interpreted with caution and emphasizes the problem of evaluating outcomes when the incidence is very low. Most of the information available for analysis was clinical history (binary variables). This does not allow for the best predictive model construction. However, in the propensity-matching analysis, 81% of the total patients and 85% of the outcomes were included. This resulted in a well-matched evaluation between the filter and non-filter groups.

Patients in this study were not assigned per a randomization scheme. Although our analysis of preoperative risk factors, demographics, and procedure category using propensity score matching account for many of the differences between groups, an even stronger case could be made in a study with a formal randomization scheme.

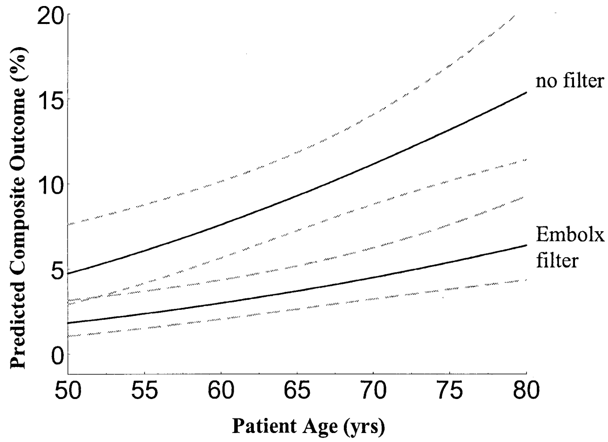

Figure 1. Model results for composite neurologic outcome for the entire population predict the probability of an outcome for patients with increasing age and no history of liver disease, myocardial infarction, or peripheral vascular disease. Predicted probabilities (solid lines); 1 SD (dashed gray lines) (70% confidence limits).

This study only looks at outcomes occurring during hospitalization. More study is needed to look at long-term effects of filtration on neurologic outcomes.

In this investigation, outcomes were assessed on a dichotomous scale; a patient was in an outcome category or not. Using graduated assessments of neurologic condition would enable more nuanced and powerful analysis.

Finally, this study looked at damage to only 1 distal organ: the brain. However, many other distal organs may be damaged by particulate emboli. In their autopsy study, Blauth and colleagues[14] reported emboli in the kidneys, gastrointestinal tract, and lower extremities. Further studies should examine intra-aortic filtration's effect on these organs. Studies are currently in progress to evaluate more subtle neurologic effects as may be detected by neuropsychologic testing.

Conclusions

This study demonstrates that in our center, the general cardiac surgery patient population benefited from significantly decreased neurologic outcomes through the use of intra-aortic filtration after all significant adjustments and after accounting for the lack of randomization. A patient without a filter during a procedure might expect a 2.7 times greater chance of experiencing an adverse outcome. Older patients seem to particularly benefit from the filter. In conjunction with earlier studies of particulate extraction, it is becoming increasingly clear that intra-aortic filtration is indicated in cases involving aortic manipulation and central anastomoses.

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Discussion

Dr H. Vanermen *(Aalst, Belgium).* In view of the fact that this was a nonrandomized study, could you give us some more detail on how patients were chosen to go into 1 arm of the study or another, and could this potentially bias the results?

Dr Schmitz. Originally we had a strict randomization scheme, but it turned out that we were not able to enroll large numbers of patients. That is why we changed our enrollment scheme in that way. All patients were enrolled preoperatively, but the treatment assignment was based on alternate time periods, and we tried to balance the numbers in both groups.

Dr Vanermen. In conjunction with earlier studies on intra-aortic filtration, what do you believe is the current understanding of the indications for use of the device?

Dr Schmitz. We had a lot of discussion about this question in our ICEM group. Most centers try to find high-risk patients for