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Timing of Stroke After Cardiopulmonary Bypass Determines Mortality

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Abstract

Background—Stroke is an important complication of cardiopulmonary bypass (CPB). This study determined if the timing of stroke events after CPB predicted stroke-related mortality or rehabilitation needs at hospital discharge.

Methods—We performed a retrospective review of 7201 consecutive cardiac surgical patients during a 10-year period and identified 202 strokes. Postoperative stroke after CPB was classified as early (≤ 24 hours) or late (> 24 hours). Data were collected on patient characteristics, intraoperative variables and outcomes, postoperative course, stroke severity, and discharge status, including death from stroke. Logistic regression analysis was used to assess the relationship between the timing of stroke and discharge status after adjusting for clinically relevant factors.

Results—The stroke incidence was 2.8%. Postoperative strokes occurred within 24 hours in 22.8% (46 of 202) and after 24 hours in 77.2% (156 of 202). Factors found in logistic regression analysis to be independently associated with stroke-related death included stroke within 24 hours postoperatively (odds ratio [OR], 9.16; $p < 0.0001$), preoperative chronic renal insufficiency (OR, 4.46; $p = 0.01$), and National Institute of Health Stroke Scale (NIHSS) score (OR, 1.16 per NIHSS point increase; $p < 0.0001$). Among survivors, early stroke was associated with greater rehabilitation needs ($p < 0.001$).

Conclusions—Early stroke after CPB is independently associated with higher stroke-related death and is associated with increased need for skilled rehabilitation at discharge. Neuroprotective strategies aimed at reducing early postoperative stroke may positively impact death and neurologic disability after CPB.

Despite numerous advances in operative technique, pharmacologic treatments, and postoperative care, stroke continues to be an important complication after procedures that use cardiopulmonary bypass (CPB) [1,2]. The estimated incidence of stroke after CPB is between 1.3% and 3.6% and depends on the type of procedure, patient age, and coexisting medical conditions [3–10].

In addition to the substantial resource utilization and economic impact of the stroke, patients and families experience a tremendous physical and psychologic burden. Several studies have used preoperative predictive modeling to better stratify those patients at risk for stroke before operation [1,2,11–18]. These studies have improved preoperative risk assessment; however,

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limited data exist on factors related to prognosis after perioperative stroke. Studies of the timing of stroke in the postoperative setting have been published [7,10,19,20]. To our knowledge, no studies to date have specifically addressed the relationship of stroke timing after CPB and neurologic outcomes.

The purpose of this study was to explore the relationship between the timing of postoperative stroke and outcome at the time of hospital discharge. Our previous institutional experience led us to hypothesize that early strokes would be associated with higher stroke-related mortality and a greater requirement for inpatient rehabilitation and skilled nursing facility utilization. Identifying factors predictive of outcome after postoperative stroke may allow clinicians to provide more accurate prognostic information to patients and families. In addition, these data may guide the development and testing of preventative strategies in patients undergoing CPB.

Patients and Methods

Patient Selection

During a 10-year period (January 1996 to December 2006), 7201 surgical procedures in adults requiring the use of CPB were performed at the University of Virginia (UVA). Individual patient data were entered into the Society of Thoracic Surgeons (STS) national database at the time of the surgical procedure. To identify potential postoperative stroke cases, an initial search of the institution-specific contribution of the STS database was performed using the following search terms: cardiopulmonary bypass, postoperative complications, stroke transient deficit, stroke exceeding 72 hours, postoperative stroke temporary, and postoperative stroke permanent. The initial search identified 256 patients, and each electronic medical record was reviewed to confirm a clinical diagnosis of postoperative stroke.

Of these, 21 patients had no documented evidence of postoperative stroke and were excluded. Also excluded were 30 patients who experienced a temporary, nonfocal, neurologic deficit attributable to another neurologic or medical cause. Diagnoses in these excluded patients included 9 with transient ischemic attacks (30%) and 21 with acute confusional states or delirium (70%). Three patients were excluded because they died of reasons unrelated to their stroke, including acute ventricular rupture in 1 and sudden cardiopulmonary failure in 2.

The final study population included 202 patients with postoperative strokes that were retrospectively confirmed by a stroke-certified vascular neurologist after review of patients' consult notes, progress notes, and radiologic studies, when available. This study was reviewed and approved by the Human Investigation Committee of the University of Virginia Health System, with a waiver of individual patient consent.

Classification of Stroke Severity

The National Institutes of Health Stroke Scale (NIHSS) score was used to grade stroke severity. The NIHSS is a validated, 15-item scale that is used to assess key components of the standard neurologic examination in stroke patients [21–24]. The scale assesses level of consciousness, ocular motility, facial and limb strength, sensory function, coordination, language, speech, and attention. Scores range from 0 (normal) to 42 (maximal deficit). Scores between 0 and 5 are generally classified as mild, and scores exceeding 15 are generally classified as severe. The NIHSS predicts short- and long-term neurologic outcomes and can be reliably abstracted from the medical record [22,23,25].

Classification of Timing of Stroke

The time of stroke was defined as either within 24 hours (early) or after 24 hours (late) after CPB. This differentiation was determined before the data were collected and was based on our

specific institutional experience as well as previous reports that a significant proportion of postoperative strokes occur within the first 24 hours after CPB [10,19]. All stroke time data were reviewed by 3 investigators, and the temporal onset of the deficits was classified by consensus as either occurring within 24 hours from the onset of the procedure (≤24-hour group) or after 24 hours from the onset of the operation (>24-hour group). If the neurologic deficit was present after the patient emerged from anesthesia or sedation, the stroke was classified as having occurred within 24 hours after operation only after the entire clinical picture was reviewed. At this point, the investigators then agreed on classification of within 24 hours. Patients were followed up until discharge from the hospital.

Patient Disposition

Patient disposition was defined as (1) death from stroke, (2) need for rehabilitation, or (3) no need for rehabilitation. Death from stroke included those patients where death was determined to be the direct result of the stroke or from stroke-related complications. This included sepsis with subsequent respiratory failure due to aspiration, hemodynamic collapse due to pulmonary embolism, brain death due to cerebral edema or herniation, and withdrawal of supportive care because of poor neurologic prognosis. Patients who were referred to skilled nursing facilities, intensive inpatient rehabilitation hospitals, or intensive outpatient rehabilitation programs after hospital discharge were classified as having rehabilitation needs. Those patients suitable for discharge to home with minimal or no assistance were classified as having no rehabilitation needs. Discharge disposition was determined by a multidisciplinary team of physicians, nurse practitioners, physician assistants, and physical, occupational, and speech therapists during the hospitalization stay and was reported in each patient's electronic medical record.

Statistical Analysis

Values are expressed as the mean ± standard deviation unless otherwise stated. All values of $p < 0.05$ were considered significant. Demographic information, past medical history items, and perioperative and operative data were tabulated. Categoric variables were compared using χ^2 analysis or the Fisher exact test, where appropriate. Continuous variables were compared using the Student *t* test. In addition to the time of stroke, variables thought to be clinically important to stroke incidence and outcome were prespecified and included in a multivariable logistic regression analysis with stroke mortality as the outcome. Time to stroke, NIHSS score, previous cerebrovascular disease, chronic renal insufficiency, CPB time, and cross-clamp time were adjusted for in the model. An independent statistician performed the analysis using SAS 9.1.3 statistical software (SAS Institute, Cary, NC).

Results

Preoperative Results

Preoperative patient characteristics are outlined in Table 1. The overall incidence of stroke in our series of 7201 patients was 2.8%. Of the 202 documented strokes, 46 (22.8%) occurred in the ≤24-hour group and 156 (77.2%) occurred in the >24-hour group. The mean age in the ≤24-hour group (65.2 ± 12.8 years) was not significantly different from the >24-hour group (68.4 ± 11.3 years). Patients in the two groups had a similar incidence of diabetes, hypercholesterolemia, peripheral vascular disease, tobacco use, chronic obstructive pulmonary disease, hypertension, renal insufficiency, known prior transient ischemic attack, known prior cerebrovascular disease, prior carotid endarterectomy, left ventricular function, and atrial fibrillation.

Operative Results

Intraoperative details are summarized in Table 2. A single-clamp technique was used in all patients. The early and late groups had similar percentages of CABG and valve procedures, respectively, at 52.2% and 28.3% in the ≤24-hour group and 61.5% and 20.5% in the >24-hour group ($p = 0.29$ and $p = 0.18$, respectively). There was a significant difference in the number of procedures performed for another pathology in addition to CABG or valvular procedures, or both. Other procedures were done in 24 patients in the ≤24-hour group (52.2%) and in 44 patients in the >24-hour group (28.2%) alone or in addition to CABG or valve procedures, or both ($p < 0.001$). Specific procedure breakdown is detailed in Table 3. When these procedures were independently evaluated relative to time course of stroke, no statistically significant differences were noted in any of the procedures.

When intraoperative variables were compared, no differences were found between the two groups in the incidence of aortic arch atheromas, use of transesophageal echocardiography, or use of epiaortic ultrasound. There were no differences in the use of alternate cannula placements, mean flow rates, hematocrit levels, or activated clotting times. Total CPB time was similar between the ≤24-hour group and the >24-hour group (143.4 ± 48.9 vs 129.0 ± 53.9 minutes, $p = 0.11$) as was aortic cross-clamp time (88.7 ± 46.2 vs 81.7 ± 42.1 minutes, $p = 0.13$).

Stroke Results

Table 4 summarizes the association between the time of stroke and stroke outcome. Strokes that occurred within 24 hours postoperatively were more severe and associated with a higher mortality. In the ≤24-hour group, median NIHSS was 16.6 ± 8.2 compared with 10.9 ± 8.3 in the >24-hour group ($p < 0.001$), demonstrating more severe strokes in the early group. Among those surviving to hospital discharge, a significantly greater proportion of patients in the ≤24-hour group (93.3%) had rehabilitation needs at the time of discharge compared with the >24-hour group (52.7%, $p < 0.001$). In the ≤24-hour group, 14 patients (30.4%) were discharged to acute rehabilitation facilities compared with 68 patients (43.6%) in the >24-hour group ($p = 0.11$). Death from stroke-related causes occurred in 31 patients (67.4%) in the ≤24-hour group vs 27 patients (17.3%) in the >24-hour group ($p < 0.001$). Table 5 details the causes of death by stroke time course. In each group, most patients with grave neurologic prognosis died after withdrawal of supportive care. In the ≤24-hour group, 25 patients (80.6%) died after withdrawal of supportive care compared with 22 (81.5%) in the >24-hour group ($p = 0.23$).

Table 6 details the results from logistic regression analysis examining the relationship of clinical variables with stroke-related mortality. Time of stroke within 24 hours, higher NIHSS score, and preexisting chronic renal insufficiency were all associated with an increased risk of death from stroke. The risk of death after stroke was 9-fold higher in patients with strokes within 24 hours postoperatively (odds ratio [OR], 9.16; $p < 0.0001$). In addition, NIHSS was shown to be independently predictive of death from stroke on a per-point basis (OR, 1.16 per point increase; $p < 0.0001$). Similarly, patients with preexisting chronic renal insufficiency had a 4.5-fold increased risk of death from stroke (OR, 4.46; $p < 0.05$).

Comment

Annually, cardiac operations using CPB are among the most frequently performed procedures in the United States. Despite improvements in preoperative risk stratification, perfusion strategies, and operative techniques, stroke continues to be a well-recognized and important postoperative complication. Our single-center, retrospective review of cardiac operations during a 10-year period found that stroke complications were infrequent. The overall stroke rate of 2.8% is similar to that reported in other studies [3–10,19].

Our data suggest that the risk of poor outcome is associated with the timing of postoperative stroke. Those who sustain a stroke within 24 hours of CPB have a greater than 9-fold risk of stroke-related death. This relationship was independent of the type of operation or stroke severity. Furthermore, preoperative chronic renal insufficiency and higher initial NIHSS scores confer an increased risk of death after strokes that occur within 24 hours of CPB.

Most studies of cardiac surgery and stroke have focused on preoperative risk assessment. Frye and colleagues [26] published their experience with preoperative prediction of stroke based on stroke time course. In their study of more than 10,000 patients, they were able to accurately predict stroke on the day of operation, during the hospitalization for the operation, or during the first postoperative year. The most powerful predictors of stroke on the day of operation were older age, use of α-adrenergic drugs after CPB, and longer duration of CPB. For those strokes occurring at least 1 day after surgery, but during the initial hospitalization, age and duration of CPB were the most powerful predictors of stroke. An analysis of predictors of stroke within 1 year after hospital dismissal for initial coronary bypass grafting (CABG) procedures revealed that the most powerful predictor was a history of previous cerebrovascular disease and a history of hypertension.

Few studies have systematically evaluated the relationship between the timing of postoperative stroke, stroke mechanism, and subsequent neurologic outcomes. Hogue and colleagues [10] detailed their findings in 2972 patients undergoing CABG or valve procedures in relationship to stroke time course and outcome. Time course of stroke was classified as either early stroke (stroke detected immediately after surgery) or delayed stroke (stroke occurred after an initial uneventful neurologic course immediately after surgery). Overall stroke rate was 1.6%, with 17 strokes (35%) in the early group and 31 (65%) in the delayed group. In multivariable logistic regression analysis, prior neurologic event, aortic atherosclerosis, and the duration of CPB were independently associated with early stroke. Delayed strokes were independently associated with prior neurologic event, diabetes, aortic atherosclerosis, and combined end points of low cardiac output and atrial fibrillation. Interestingly, history of stroke was the strongest predictor of perioperative stroke, regardless of whether strokes were considered as a single time point or whether early and delayed strokes were considered separately.

In-hospital mortality for early (41%) and delayed strokes (13%) was significantly higher than that for patients without postoperative stroke. The proportion of patients with early and late postoperative stroke in our cohort is in keeping with the findings of Hogue and colleagues [10]. Although a direct statistical comparison between the mortality rates for early and late strokes are not presented in their study, the difference in proportions suggests a significantly higher mortality rate for early strokes. These studies did not adjust for the confounding effect of stroke severity, however, which has been established as a strong predictor of outcome [22].

The significantly increased risk of poor outcome in those with early postoperative stroke identified in our data may be attributable to a difference in the underlying stroke mechanism between early and late postoperative stroke. Many authors agree that strokes after the use of CPB are largely the result of hypoperfusion injury or thromboembolic insults [11,19,20]. Very few strokes, if any, in the post-CPB setting are the result of hemorrhage alone. Likosky and colleagues [19] published their findings of stroke etiology in 388 patients that sustained a stroke after CPB. They found that thromboembolic strokes accounted for more than 66% of the total strokes, whereas hypoperfusion related strokes accounted for less than 10%. Another 10% of their patients sustained strokes that resulted from more than one cause, and 14% were left unclassified. Similarly, Hogue and colleagues [10] found that nearly two-thirds of their strokes were the result of embolism, and one-third were the result of hypoperfusion alone. Interestingly, when stroke mechanism was stratified by time of stroke, the results were similar. In the early

group, 65% of the strokes were the result of an embolic mechanism, whereas strokes due to hypoperfusion accounted for 29%. In the delayed group, embolic strokes accounted for 58% of the total strokes and 36% were due to hypoperfusion.

Despite substantial evolution in both operative and perfusion techniques, embolization continues to be a serious problem during CPBs. Embolic particles may be solid (eg, thrombotic, lipid, or atheromatous), originating from direct aortic manipulation or gaseous, resulting largely from open cardiac procedures. Even with the introduction of widespread epiaortic scanning and intraoperative transesophageal echocardiography, as well as modified aortic clamping techniques, inline arterial filters, and intraaortic filters, embolic matter continues to be an important source of stroke after CPB [10].

Prolonged periods of hypoperfusion place patients at increased risk of ischemic insults during operation as well, even with advances in anesthetic technique, introduction of vasoactive drugs, and increasingly invasive monitoring techniques. It is well known that older patients and those with hypertension and diabetes may be at increased risk of hypoperfusion events owing to their lack of adequate autoregulatory mechanisms within the cerebral circulation [10]. Moreover, the ideal level of arterial blood pressure during CPB remains a debatable topic, and the few existing studies have not resulted in definitive conclusions about optimal blood pressure management [27,28].

Limitations inherent to a retrospective design were encountered in this study. In some cases, incomplete documentation of the time of symptom onset or the confounding effects of sedation/anesthesia on the clinical examination may have resulted in misclassification with regard to stroke timing. We attempted to minimize misclassification through medical record review by 3 investigators and by using a consensus method to categorize stroke timing. We have no reason to suspect that our study results or conclusions have been biased through differential misclassification of early vs late stroke.

The results of ancillary tests such as echocardiography, cervical and intracranial vascular imaging, and brain magnetic resonance imaging were not available in all patients. Such testing is necessary to accurately determine the most likely stroke mechanism. This inconsistency was the result of variability in stroke evaluation of the treating physician or team. For this reason, we were unable to incorporate data on stroke mechanism or radiologic findings as they relate to timing of stroke and outcomes. However, the absence of this additional information does not influence the fundamental observations of this study. Prospective studies would benefit from the use of standardized preoperative and postoperative neurologic assessments and a standardized battery of ancillary tests to improve diagnostic accuracy.

The heterogeneous nature of surgical procedures experienced by our population limited the power to explore the relationship between the type of operation and stroke outcome. Stroke-related death in this study included patients where withdrawal of care ultimately resulted in death. Although we cannot definitely establish if these patients would have died of another medical complication had care not been withdrawn, the decision to withdraw care in all cases was due to grave neurologic prognosis, which we believe is a reasonable surrogate for stroke-related death. Lastly, we acknowledge the potential for unknown or unmeasured confounding variables within our data set that we were unable to control for through statistical measures.

Our finding that early stroke is independently associated with higher stroke-related death may have both prognostic and therapeutic implications. If other investigators confirm this association, the timing of a postoperative stroke diagnosis may provide patients and families with important prognostic information as well as insight into anticipated resource utilization such as skilled nursing or home health care.

Importance however rests in determining the true association between the time of stroke after CPB, the mechanisms of these strokes, the characterization of subsequent clinical and radiologic patterns, and clinical outcomes. These data may provide a foundation for future pilot clinical trials of neuroprotectant drugs in the perioperative period. On the basis of these data, preventative strategies using 3-hydroxy-3 methyl-glutarylcoenzyme A (HMG-CoA) reductase inhibitors or other putative neuroprotectant drugs in the CPB surgical population should be focused on the preoperative and early postoperative time period.

Appendix

DISCUSSION

DR PETER K. SMITH (Durham, NC): I want to congratulate you, Dr Lisle, on an excellent study and excellent presentation. Obviously this is a devastating complication and you have reiterated for us the lethality of it, particularly in the early stroke victims, and ultimately the unsatisfactory conclusion for almost all of these patients regardless with a lot of rehabilitation and loss of quality of life.

I would like to ask you basically three questions. It is useful when you are dealing with a problem like this that is a low probability event, but highly lethal, to have an understanding prospectively of who these patients are. So I would ask if you looked at the remaining patients —that is, those patients who had not had a stroke—in order to be able to identify those patients that ultimately did have these complications and compare them? I noticed that your preoperative atrial fib rate, for example, was quite high, about 18% to 25%, and although it is a mixture of patients with valvular heart disease, the incidence is only about 2% or 3% in coronary bypass patients. So I was wondering if that was a particular predictor.

The second thing I would like to ask you is, obviously, you have a 10-year experience, and during that 10 years, this complication has become much more highly recognized and a number of techniques have changed over time, including using a single-clamp technique, epiaortic scanning, and even the introduction of statin agents, as you have demonstrated in other research, and I was wondering if you have had a chance to see if any of these things have had an impact or if there is sufficient data in your data set to be able to do such a thing?

And then clearly, the incidence of late stroke suggests that postoperative management in these patients could be adjusted, and I wonder if you might speculate as to what could be done, because obviously we have an opportunity to prevent stroke by other than selecting patients. And in particular, I wonder if you noticed any correlation between postoperative atrial fib, antiplatelet therapy or any anticoagulant therapy, or if you have considered changing these things in the practice? Thank you.

DR LISLE: Thank you for your comments, Dr Smith. To answer your first question, we did not compare this group of patients to a cohort that did not have strokes, because what we were really interested in was finding out where we are going to get the most bang for our buck in terms of treating patients that have strokes. We have certainly been able to demonstrate with this study that those patients who suffer strokes either intraoperatively or shortly thereafter are at a higher risk for bad complications, including death and intensive rehabilitation. Based on this, we feel that these early strokes should be a special focus for further research. In terms of comparisons in general, several groups have previously addressed this issue, so we felt less inclined to do this same kind of analysis; however, being a retrospective study, it is certainly something we could take a look at in the future.

To answer your second question, how we handle these patients intraoperatively, we use a single-clamp technique on all of our patients. If we have someone who appears to have a

severely diseased aorta, we use selective epiaortic ultrasound. If our evaluation shows the severe disease we expected, then we use alternate cannula placements exclusively, including both axillary and femoral locations.

In terms of postoperative management, we did not look specifically at whether or not patients were treated with statins or were treated with anticoagulation or antiplatelet agents. I don't know exactly what the impact of those treatments was in the postoperative setting, but it is certainly something that would be interesting to look at in future prospective studies.

DR WILLIAM A. BAUMGARTNER (Baltimore, MD): I thought it was a really nice presentation. I have a question. You could speculate that early strokes are related to perhaps increased anticoagulation following bypass in that first 24 hours. But if that were of the case, you would have observed that in your computed tomography scans or your magnetic resonance images (MRIs). I was wondering if you looked at those and tried to correlate them in these patients both within the first postoperative 24 hours and beyond 24 hours?

DR LISLE: One of the hard things to do in a retrospective study like this is to look at the data that you have and be able to come up with a complete data set. One of the difficult things that we found looking back at some of these patients was that we were unable to accurately classify stroke mechanism, and so we lumped all kinds of strokes into one single group. It has been shown very well in the literature that the vast majority of the strokes that occur in the perioperative period are either thromboembolic or hypoperfusion in nature, and I can tell you that the patients in our study whom we were able to accurately determine stroke etiology had similar distributions to what is reported elsewhere. There was a study that was published a while back that actually looked at the incidence of thromboembolic events and hypoperfusion events and showed no difference in time points either initially postoperatively or up to 20 days postoperatively, and our results for the most part were similar to this work.

I think one key factor is to be able to look at this sort of thing prospectively, in order to be able to determine how stroke mechanism truly influences mortality and eventual outcome. We hope to do that in the near future.

DR MARC MOON (St. Louis, MO): It seems to me that some of those strokes within the first 24 hours you probably may not have recognized for a couple of days and by then the cat is out of the bag; whereas, if a stroke occurs at 4 or 5 days, that is maybe something you can address at that point.

DR JOHN W. HAMMON JR (Winston-Salem, NC): I really appreciate the fact that these strokes were all clinically verified by a neurologist, I think that is very important, rather than using the surgical team. I think in the recent time when we have started to look at MRI data in postoperative patients, particularly using a technique called diffusion-weighted imaging that allows you to determine the time course of the stroke, that most postoperative strokes have multiple lesions on MRI, and the number and size of the lesions is pretty much directly related to the severity of the stroke. So I have a hypothesis, and maybe we can all work to prove it. It is that the patients that have the less severe delayed strokes have fewer and smaller lesions that become clinically apparent later on only when they become edematous and cause some trouble in terms of symptoms; but, at this point, that is just speculation.

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Table 1

Clinical Profile Stratified by Timing of Stroke

Characteristic	Time to Stroke[a]		*p* Value[b]
	≤24 Hours	>24 Hours	
Patients, total	46	156	
Male	28 (60.9)	88 (56.4)	0.59
Age, years	65.2 ± 12.8	68.4 ± 11.3	0.11
Diabetes mellitus	13 (28.3)	55 (35.2)	0.38
Hypercholesterolemia	20 (43.5)	69 (44.2)	0.93
Peripheral vascular disease	8 (17.4)	20 (12.8)	0.43
Tobacco use	21 (45.6)	65 (41.6)	0.31
COPD	18 (39.1)	53 (33.9)	0.32
Hypertension	29 (63.0)	103 (66.0)	0.71
Chronic renal insufficiency	11 (23.9)	29 (18.9)	0.43
Prior TIA	5 (10.9)	9 (5.8)	0.32
Cerebrovascular disease	12 (26)	35 (22.4)	0.61
Prior CEA	2 (4.3)	8 (5.1)	1.00
Presence of carotid bruit	4 (8.7)	20 (12.8)	0.45
Preoperative LV function			
Normal	29 (63.0)	86 (55.2)	
Mild dysfunction	7 (15.2)	32 (20.5)	0.69
Moderate dysfunction	5 (10.9)	25 (16.0)	
Severe dysfunction	5 (10.9)	13 (8.3)	
Atrial fibrillation	8 (17.4)	37 (23.7)	0.36

COPD = chronic obstructive pulmonary disease; CEA = carotid endarterectomy; LV = left ventricular; TIA = transient ischemic attack.

[a] Continuous variables are reported as mean ± SD, and categoric variables are reported as number (%)

[b] Student *t* test, χ^2 test, or Fisher exact test, where appropriate.

Table 2

Operative Details Stratified by Timing of Stroke

Detail	Time to Stroke[a]		p value[b]
	≤24 Hours	>24 Hours	
Patient, total	46	156	
Procedure			
CABG	24 (52.2)	96 (61.5)	0.29
Valve repair/replacement	13 (28.3)	32 (20.5)	0.18
Other[c]	24 (52.2)	44 (28.2)	<0.001
Aortic arch atheroma	7 (15.2)	9 (5.7)	0.06
Post-op antifibrinolytics	1 (2.2)	0 (0)	0.23
TEE or epiaortic US	3 (6.5)	5 (3.2)	0.39
Alternate arterial cannula	3 (6.5)	3 (1.9)	0.13
HCA	7 (15.2)	20 (12.8)	0.23
Average flow rate			
Initial	4.4 ± 1.1	4.4 ± 0.7	0.52
Midpoint	3.8 ± 1.1	4.0 ± 0.8	0.26
Final	4.4 ± 1.1	4.6 ± 0.9	0.28
Hematocrit			
Pre-CPB	38.4 ± 6.1	38.2 ± 5.6	0.83
Initial	22.1 ± 6.0	22.4 ± 5.4	0.75
Midpoint	22.4 ± 5.0	22.6 ± 3.4	0.80
Final	22.9 ± 4.2	23.4 ± 3.5	0.50
Activated clotting time			
Initial	551.9 ± 239.8	513.2 ± 187.1	0.33
Midpoint	673.1 ± 244.2	645.5 ± 190.2	0.50
Final	623.9 ± 230.2	583.6 ± 183.5	0.23
Total CPB time, min	143.4 ± 48.9	129.0 ± 53.9	0.11
Cross-clamp time, min	88.7 ± 46.2	81.7 ± 42.1	0.13

CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass; HCA = hypothermic circulatory arrest; TEE = transesophageal echocardiography; US = ultrasound.

[a] Continuous variables are reported as mean ± SD, and categoric variables are reported as number (%)

[b] Student *t* test, χ^2 test, or Fisher exact test, where appropriate

[c] Refer to Table 3 for specific procedure breakdown.

Table 3

Other Operative Procedures Stratified by Timing of Stroke

Other Procedures	Time to Stroke, No. (%)		*p* Value[a]
	≤24 Hours	>24 Hours	
Patient, total	46	156	
Thoracic aortic aneurysm repair	8 (17.4)	14 (8.9)	0.11
Type I aortic dissection repair	4 (8.7)	5 (3.2)	0.11
Carotid endarterectomy	2 (4.3)	7 (4.5)	0.66
Orthotopic heart transplant	2 (4.3)	3 (1.9)	0.32
ASD/VSD closure	2 (4.3)	5 (3.2)	0.66
LVAD placement	2 (4.3)	5 (3.2)	0.66
Aortic root replacement	2 (4.3)	3 (1.9)	0.92
PDA ligation	1 (2.2)	0 (0)	0.23
Left ventricular aneurysm repair	1 (2.2)	0 (0)	0.23
Intraaortic balloon placement	0 (0)	1 (0.6)	1.00
Descending aneurysm repair	0 (0)	1 (0.6)	0.23

ASD/VSD = atrial septal defect/ventricular septal defect; LVAD = left ventricular assist device; PDA = patent ductus arteriosus.

[a] Student *t* test, χ^2 test, or Fisher exact test, where appropriate.

Table 4

Stroke Details Stratified by Timing of Stroke

Detail	Time to Stroke[a]		*p* Value[b]
	≤24 Hours	>24 Hours	
Patient, total	46	156	
NIHSS[c]	16.6 ± 8.2	10.9 ± 8.3	0.0002
Length of stay			
ICU	12.2 ± 12.0	9.2 ± 13.0	0.22
Hospital	28.1 ± 36.9	20.4 ± 22.5	0.21
Disposition			
No rehabilitation	1 (2.2)	61 (39.1)	<0.001
Rehabilitation	14 (30.4)	68 (43.6)	0.11
Death	31 (67.4)	27 (17.3)	<0.001

ICU = intensive care unit; NIHSS = National Institute of Health Stroke scale.

[a] Continuous variables are reported as mean ± SD, and categoric variables are reported as number (%)

[b] Student *t* test, χ^2 test, or Fisher exact test, where appropriate

[c] Median value ± interquartile range (25th and 75th percentiles) represented for NIHSS.

Table 5

Causes of Death Stratified by Timing of Stroke

Cause of Death	Time to Stroke, No. (%)		*p* Value[a]
	≤24 Hours	>24 Hours	
Patient, total	31	27	
Withdrawal of supportive care due to poor neurologic prognosis	25 (80.6)	22 (81.5)	0.23
Aspiration with resultant respiratory failure	3 (9.7)	2 (7.4)	0.15
Intracranial herniation and brain death	3 (9.7)	2 (7.4)	0.15
Pulmonary embolism and resultant hemodynamic collapse	0 (0)	1 (3.7)	0.12

[a] Student *t* test, χ^2 test, or Fisher exact test, where appropriate.

Table 6

Multivariable Logistic Regression Analysis Examining Independent Influence of Clinically Relevant Factors to Mortality After Stroke

Factor	OR	95% CI	*p* Value
Time to stroke			
≤24 hours	9.16	3.4–24.6	<0.0001
>24 hours	1.0[a]	. . .	. . .
NIHSS, per point	1.16	1.09–1.23	<0.0001
Cerebrovascular disease	0.43	0.14–1.33	0.14
Chronic renal insufficiency	4.46	1.40–1.33	0.01
CPB time, per min	1.00	0.99–1.02	0.58
Cross-clamp time, per min	0.99	0.98–1.01	0.47

R^2 = 0.35, *c* statistic = 0.874.

CI = confidence interval; CPB = cardiopulmonary bypass; NIHSS = National Institute of Health Stroke scale; OR = odds ratio.

[a]Referent group.