Large-vessel occlusion stroke after cardiothoracic surgery: Expanding time windows offer new salvage opportunities

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ABSTRACT

Objectives: Ischemic stroke due to large-vessel occlusion (LVO) is a complication after cardiothoracic surgery (CTS). Recently published endovascular stroke trials have major implications for treating LVO strokes; we evaluated our experience in patients undergoing CTS.

Methods: Our prospective institutional CTS database was reviewed between July 2013 and April 2018 for ischemic strokes. Patients with LVO were identified and their course and outcomes analyzed.

Results: A total of 5947 patients were reviewed; 148 (2.48%) had a cerebrovascular complication; 92.5% were ischemic. Of these 10.9% had an LVO. Prolonged aortic crossclamp was associated with LVO (odds ratio, 1.012 for every minute of prolonged aortic crossclamp time; confidence interval, 1.001-1.023) and remained significant in patients with ejection fraction >45%; prolonged cardiac bypass time was only associated with LVO in patients with ejection fraction >45% (odds ratio, 1.012 for every minute of prolonged cardiac bypass time; confidence interval, 1.003-1.021). Patients fell into 2 categories: detection of neurologic deficit in the stable postoperative patient or detection of deficit on emergence from anesthesia. Seven patients met criteria for emergent revascularization, with median National Institutes of Health Stroke Scale score 15, and shorter times from last seen well to deficit detection compared with patients not meeting criteria ($P = .032$). Median National Institutes of Health Stroke Scale day 7 score improved to 5. There was a trend toward better modified Rankin Scale scores at 3 months in patients who underwent thrombectomy.

Conclusions: LVO complicates a small proportion of patients after CTS and may be more likely with prolonged aortic crossclamp and cardiac bypass times. Both early and late window endovascular stroke treatment has the potential to positively modify the complication profile of CTS. Greater awareness of this treatment option is needed. (J Thorac Cardiovasc Surg 2019;158:186-96)

Pre- and post-thrombectomy angiograms for large-vessel occlusion with successful reperfusion.

Central Message

Large-vessel stroke as a complication of cardiac surgery now has evidence-based treatment up to 24 hours from last known normal. Awareness among providers is paramount to ensure optimal patient care.

Perspective

Cardiothoracic surgery can be complicated by large-vessel ischemic stroke; this unique population had no significant representation in stroke thrombectomy trials. We describe a large cohort of such patients, demonstrating the feasibility of mechanical thrombectomy and specific technical and logistic challenges faced. Awareness of this new treatment opportunity is key to timely mobilization of resources.

See Commentaries on pages 197 and 199.

Ischemic stroke complicates cardiothoracic surgery (CTS) and is associated with greater morbidity, mortality, readmission, and impaired quality of life.¹ Although the risk factors

predisposing patients undergoing CTS to neurologic complications and ischemic stroke have been described,^{1,2} there is paucity of data regarding large-vessel occlusion (LVO) strokes. This subtype of ischemic stroke causes the majority of the death and severe disability from stroke and therefore has devastating consequences if the occlusion remains untreated.^{3,4}

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Scanning this QR code will take you to the article title page to access supplementary information.

Abbreviations and Acronyms

ACC	= aortic crossclamp
ASPECTS	= Alberta Stroke Program Early CT Score
CABG	= coronary artery bypass graft
CEA	= carotid endarterectomy
CI	= confidence interval
CPB	= cardiac bypass
CT	= computed tomography
CTA	= computed tomography angiography
CTICU	= cardiothoracic intensive care unit
CTS	= cardiothoracic surgery
EF	= ejection fraction
ICA	= internal carotid artery
LSW	= last seen well
LVO	= large-vessel occlusion
MCA	= middle cerebral artery
MR	= magnetic resonance
mRS	= modified Rankin scale
mTICI	= modified Thrombolysis in Cerebral Infarction
NIHSS	= National Institutes of Health Stroke Scale
OR	= odds ratio

The basic tenet of all acute stroke treatment is reperfusion, removing the obstruction of the cerebral vessel to restore blood flow and preserving threatened cerebral tissue. Thrombectomy devices are essential in the treatment of LVO stroke, as they provide a mechanical means of clot extraction, and have evolved steadily over the past 2 decades, with new terminology ([Appendix E1](#)). In 2015, 5 major trials were published that established the superiority of mechanical thrombectomy over medical therapy (intravenous thrombolytic with alteplase) alone in patients presenting within 6 hours of stroke onset.⁵

However, there is often a long duration between last known well times and symptom discovery for patients undergoing CTS. LVO stroke presenting in late time windows (ie, beyond 6 hours) was until recently regarded as a complication of CTS without evidence-guided treatment. This has changed with the recently published DAWN (DWI or CTP Assessment With Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo) and DEFUSE 3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke) trials.^{3,4} Enrolling patients with severe neurologic compromise, one half of patients undergoing endovascular stroke therapy in these trials returned to functional independence by 90 days. These trials also

demonstrated exceedingly poor outcomes in the medical arm, underscoring the poor natural history of the disease (and producing the largest treatment effect in the history of stroke trials). This has opened endovascular stroke therapy to patients with LVO stroke who were previously ineligible for thrombectomy based on time criteria alone, including “wake-up” strokes following CTS. In view of this, we explored the incidence of LVO in our CTS population and detail our experience with LVO post CTS in both “early” (<6 hours) and “late” (6–24 hours) windows.

METHODS

Patient Population

Prospectively maintained institutional CTS and stroke databases were reviewed for all cerebrovascular complications between July 2013 and April 2018. Any cerebrovascular complication within 30 days of the procedure was further classified as ischemic or hemorrhagic based on noncontrast computed tomography (CT) of the head or brain magnetic resonance (MR) imaging and stroke neurology evaluation. Ischemic strokes were then further classified according to presence of LVO noted on CT or MR angiography.

Patient Categorization

LVO was defined as occlusion of either the terminal internal carotid artery (ICA) or proximal middle cerebral artery (MCA; M1 or M2), or basilar artery on CT or MR angiography. Candidacy for thrombectomy was determined by LVO with an associated clinical stroke syndrome severe enough for a National Institutes of Health Stroke Scale (NIHSS) score ≥ 6 . These patients were compared with the patients with ischemic stroke without documented LVO on vessel imaging; data on vascular risk factors, cardiothoracic surgery subtype, cardiac bypass (CBP), and aortic crossclamp (ACC) times were collected.

Patient Treatment

Patients with LVO were evaluated for mechanical thrombectomy per institutional protocol ([Appendix E2](#)); if eligible, this was performed emergently. They were then followed by the stroke service. The modified Rankin Scale (mRS), a scale assessed at 3 months for functional independence after stroke, was retrospectively calculated from chart follow-up.

Statistical Analysis

Statistical analysis was performed using SPSS, version 21 (IBM Corp, Armonk, NY). Explanatory variables were divided into either continuous or categorical variables. Comparison of outcomes between groups using continuous variables was performed using independent-samples *t* test if the variables were normally distributed. For non-normally distributed variables, these were log-transformed to achieve normal distribution. Values were expressed as mean ($\pm$ standard error of mean) for normally distributed variables, or median (interquartile range) for skewed deviations. Comparison between groups using categorical variables was done using the χ^2 or Fisher exact tests. The association between the explanatory variables and the outcomes of interest was assessed using binary logistic regression.

RESULTS

Stroke Incidence

Records of a total of 5947 patients were reviewed in the CTS database. Of these 148 (2.48%) had a cerebrovascular complication within 30 days. These patients had undergone

a wide range of procedures, including aortic arch repair (37.9%), mitral valve repair or replacement (22.8%), coronary artery bypass graft (CABG) (15.9%), aortic valve repair or replacement (14.5%), and mechanical circulatory device insertion (9%), with some having more than 1 procedure. The mean ejection fraction (EF) preprocedure in the ischemic stroke subgroup was 55.7%. The mean ACC and CBP times were 113.1 minutes and 158.2 minutes, respectively, in the ischemic stroke subgroup. The prevalence of vascular risk factors was as follows: hypertension (69.9%), hyperlipidemia (58.9%), smoking (52.1%), atrial fibrillation (28.1%), and previous stroke (13.7%).

LVO Stroke

Of the 148 patients with stroke, there were 137 ischemic strokes (92.5%) and 11 intracranial hemorrhages (7.5%). Of the 137 patients with ischemic stroke, 119 had vessel imaging, with 15 documented LVO cases (12.6% of the ischemic stroke population that underwent vessel imaging). The most common site of occlusion was proximal

MCA (M1 and M2 divisions) followed by ICA terminus. Twelve of these 15 patients with LVO had a clinical deficit significant enough for thrombectomy consideration (8.1% of the total stroke population, 8.8% of the ischemic stroke population). Of these, 6 were eligible for endovascular therapy and 1 for emergent carotid endarterectomy (CEA) based on NIHSS, favorable Alberta Stroke Program Early CT Score (ASPECTS), LVO, and collateral profile (Figure 1).

Baseline age, sex, and cardiac variables including EF and subtypes of cardiothoracic surgery were similar in the LVO versus non-LVO ischemic stroke groups. Patients with LVO ischemic stroke compared with patients without LVO had longer mean CPB times (193.6 vs 154.5 minutes), mean ACC times (158.8 vs 111.5 minutes), and mean deep hypothermic circulatory arrest times (48.7 vs 27 minutes) (Table 1). Procedures associated with LVO were distributed as follows: circulatory assist devices (20%), mitral valve (8.0%), aortic root or arch repair (7.7%), aortic valve (8.9%), and CABG (2%).

FIGURE 1. Flow diagram representing patients analyzed in the cardiothoracic surgery database with cerebrovascular complications. (Percentages are calculated based on the preceding patient subpopulation.) *NIHSS*, National Institutes of Health Stroke Scale.

TABLE 1. Baseline characteristics for ischemic stroke patients after CTS, by LVO status

Patient characteristics	LVO with significant clinical deficit (n = 12)	Non-LVO* (n = 125)	P value
Age, y, mean (SEM)	61.8 (3.35)	67.1 (0.89)	.09
Sex, % males	75%	57.1%	.36 (Fisher exact)
Procedure subtype			
Circulatory assist devices	20.0%	7.8%	.29
Mitral valve repair/replacement	8.0%	8.8%	.19
Aortic root/arch repair	7.7%	9.1%	.46
Aortic valve repair/replacement	8.9%	8.5%	.79
CABG	2.0%	12.4%	.10
Ejection fraction, mean (SEM)	51.4% (5.47)	55.7% (1.54)	.39
ACC time, min, mean (SEM)	158.8 (29.2)	111.5 (5.5)	.034
ACC time for EF >45%, min (SEM)	167.1 (32.4)	110.8 (6.1)	.029
CBP time, min (SEM)	193.6 (38.6)	154.52 (6.8)	.122
CBP for EF >45%, min (SEM)	251.3 (48.6)	154.48 (7.7)	.008
DHCA, min (SEM)	48.7 (24.4)	27.0 (3.3)	.123
Risk factors			
Previous stroke	18.2%	13.8%	.66
HLD	36.3%	60.7%	.12
Smoking	41.6%	52%	.56
Afib	27.3%	27.6%	.9
Diabetes mellitus	41.6%	31.6%	.15
HTN	45.4%	72.3%	.09

LVO, Large-vessel occlusion; SEM, standard error of the mean; CABG, coronary artery bypass graft; ACC, aortic crossclamp; EF, ejection fraction; CBP, cardiac bypass; DHCA, deep hypothermic circulatory arrest; HLD, hyperlipidemia; Afib, atrial fibrillation; HTN, hypertension. *Includes patients who had no vessel imaging and clinical syndrome incompatible with LVO (n = 18) and patients with partially occlusive LVO without significant clinical deficit (n = 3).

On univariate analysis, there was an association between ACC time and LVO (odds ratio [OR], 1.011 for each minute of increased ACC time; confidence interval [CI], 1.001-1.021, $P = .036$). There was also a trend toward an association between prolonged CPB time/deep hypothermic circulatory arrest times and LVO that did not reach significance ($P = .122$ and $.123$, respectively). When patients were dichotomized per EF, there remained a significant association between prolonged ACC times and LVO in patients with EF >45%. (OR, 1.012 for every minute of prolonged ACC time; CI, 1.001-1.023). In addition, there was a significant association between prolonged CBP time and LVO in patients with EF >45%. (OR, 1.012 for every minute of prolonged CBP time; CI, 1.003-1.021; Table 1). Multivariate analysis was not performed because of the limited number of patients with LVO. The mean time from last seen well (LSW) to imaging was 6.2 hours in the group that underwent thrombectomy and 38.4 hours in the group that did not ($P = .032$). Nine of 12 patients presented within 24 hours; of these, 6 presented within the 6-hour window.

Thrombectomy Results

Patients who underwent mechanical thrombectomy ranged from 37 to 70 years of age and were all male

patients. The cardiac procedures performed in this thrombectomy group included ventricular assist device placement (3 patients) and aortic arch or valve repair/replacement (4 patients), with 1 patient having both performed. In addition, 1 patient had a recent CABG and contralateral CEA (Tables 2 and 3).^{15,16}

Patients with LVO fell into 2 categories: the first were “wake-up” patients who had detection of deficit on emergence from anesthesia. These were patients placed on cardiopulmonary bypass, cooled for direct cardiac manipulation, and then decannulated from bypass and gradually warmed before transfer to the cardiothoracic intensive care unit (CTICU) for weaning of sedation. Neurologic deficit was detected in the CTICU on weaning from sedation. The median time from LSW to detection in this subgroup was 750 minutes. Case 1, to follow, is representative of this subgroup. The second group comprised awake patients who had new-onset deficits following initial uneventful emergence from the procedure. The median time from LSW to detection in this subgroup (among thrombectomy patients) was 67.5 minutes. Case 5 mentioned herein represents this subgroup.

All 7 patients who had LVO and underwent revascularization had left heart endocardial manipulation

TABLE 2. Patient demographics, stroke, and outcomes data for LVO patients who underwent thrombectomy

Case	Age	Baseline mRS*	Cardiac surgery type	EF (%)	ACC time, min	CBP time, min	NIHSS at onset*	Initial ASPECTS*	LSW to detection, min
LSW >6 h									
1	53	3	LVAD placement, TV repair	13	–	130	20	8	720
2	37	1	Aortic valve replacement and arch repair for aneurysm	72	81	146	24	7	780
LSW ≤6 h									
3	67	1	Elective TAVR (at an outside hospital)	70	–	–	16	9	15
4	53	3	Previous BiVAD placement	32	–	77	7	8	120
5	70	0	Mitral valve replacement, maze procedure	65	125	176	7	7	150
6	70	3	Previous LVAD placement, previous CABG	25	–	82	15	9	10
7	61	0	CABG	45	100	109	13	10	30

mRS, Modified Rankin Scale; EF, ejection fraction; ACC, aortic crossclamp; CBP, cardiac bypass; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; LSW, last seen well; CTA, computed tomography angiography; mTICI, modified Thrombolysis in Cerebral Infarction; LVAD, left ventricular assist device; TV, tricuspid valve; CASPER, combined aspiration and stentriever²²; ADAPT, A Direct Aspiration First-Pass Technique²³; PH2, parenchymal hematoma type 2; TAVR, transcatheter aortic valve replacement; SAH, subarachnoid hemorrhage; BiVAD, biventricular assist device; HII, hemorrhagic infarction type 1; ICA, internal carotid artery; CABG, coronary artery bypass graft; CEA, carotid endarterectomy. *Please see [Appendix E1](#) for details on these stroke scoring systems and classifications.

except for 1 patient with recent CABG. Of these, 6 underwent mechanical thrombectomy and 1 had emergent CEA. NIHSS score at presentation ranged from 7 to 20 (median 15). ASPECTS on initial CT head ranged from 7 to 10 (median 8). CT angiography revealed 5 proximal (M1) occlusions, 1 ICA terminus occlusion, and 1 M2 occlusion (ie, distal to the bifurcation of MCA in the Sylvian fissure). Time from groin puncture to reperfusion ranged from 16 minutes to 1 hour, 57 minutes with 4 of 6 thrombectomy patients attaining goal modified Thrombolysis in Cerebral Infarction (mTICI) score 2b/3 recanalization (reperfusion of 50% of the territory threatened by ischemia or more; see [Appendix E1](#) for mTICI scoring). Clot pathology was available for 2 patients; one had “disorganized thrombus” and the other “mature adipose tissue.” The endovascular techniques used included direct aspiration (A Direct Aspiration First-Pass Technique) and stentriever thrombectomy. Stentriever use was always in combination with aspiration (combined aspiration and stentriever use).⁶

Noncontrast CT of the head at 24 hours postprocedure showed subarachnoid hemorrhage in 2 patients and intraparenchymal hemorrhage in 2 patients; 1 of the latter 2 also had evidence of early cerebral edema later requiring hemicraniectomy. One patient had a small procedural ICA dissection that resolved without sequelae.

Postprocedure, 6 patients were transferred to a cardiac critical care unit and 1 patient was admitted to a neurocritical care unit. NIHSS at 1 week was median 5

(improved from preprocedure median of 15). The median follow-up mRS in the thrombectomy group at 2 months postprocedure was 3, primarily driven by underlying cardiac comorbidities; of note, 1 patient died from surgical wound-related complications unrelated to their stroke. In comparison, the median mRS in the nonthrombectomy group was 4 with 2 deaths, both related to herniation syndromes from malignant cerebral edema and subsequent withdrawal of care. Patients who underwent thrombectomy had a trend toward better delta mRS scores (computed from the difference between admission and 3-month mRS scores) compared with patients who did not undergo emergent revascularization ($P = .09$).

Of the patients undergoing intervention, all 7 occurred after the publication of the 2015 stroke trials. “Wake-up” LVO treatment occurred only after release of the DAWN results.

CASE EXAMPLES

Case 1

A 53-year-old man with nonischemic cardiomyopathy due to Becker muscular dystrophy underwent uneventful left ventricular assist device placement and tricuspid valve repair; on lifting sedation in the CTICU, he exhibited a right MCA syndrome with NIHSS 20 at 7 hours, 15 minutes after ventricular cannulation. Time from LSW (preinduction) to symptom detection was 12 hours. Following activation of the stroke service, initial CT of the head showed an ASPECTS of 9 (indicating minimal established infarct); computed tomography angiography (CTA) and conventional angiography demonstrated a proximal right M1 MCA cutoff ([Figure 2, B](#)). Time from LSW to groin puncture was

TABLE 2. Continued

LSW to CTA, min	Groin puncture to recanalization, min	Intra-arterial therapy result (mTICI)	Clot path (if available)	Device(s) used	Complications	NIHSS day 7	Change in mRS at last follow-up
937	117	2b	Disorganized thrombus	CASPER ×3	None	9	0
950	16	2b	Unavailable	ADAPT ×1	PH2*	21	+3
77	43	2b	Unavailable	ADAPT ×2 CASPER ×2	Trace SAH	7	+2
139	56	2a	Unavailable	ADAPT ×1 CASPER ×3	None	0	Death (unrelated to stroke)
207	81	2a	Mature adipose tissue	ADAPT ×2 CASPER ×2	HI1,* small ICA dissection	5	+2
86	19	2b	Unavailable	ADAPT ×1	Trace SAH	1	-1
97	CEA	—	—	—	None	2	+2

16 hours, 20 minutes. mTICI 2b recanalization was achieved in 1 hours, 57 minutes (Figure 2, C and D). Clot pathology was consistent with disorganized thrombus. A 24-hour CT of the head showed hypodensities in the caudate head and lentiform nucleus (Figure 2, E). NIHSS at 1 week was improved to 9. He was discharged to a rehabilitation facility and eventually home. His mRS at 3 months was 3 (able to ambulate with assistance), which was his baseline before the procedure.

Case 5

A 70-year-old man was admitted for atrial fibrillation with rapid ventricular response and severe mitral regurgitation and underwent mitral valve replacement and maze procedure for ablation. Immediately postprocedure, he was neurologically intact; however, a right MCA syndrome developed (NIHSS 7) at 15 hours, 30 minutes post-onset of procedure; the time from LSW to diagnosis was 2 hours, 30 minutes. CT of the head showed early ischemic changes with hypodensity in M1 (Figure 3, A); CTA showed right M1 occlusion. (Figure 3, B). Time from LSW to groin puncture was 4 hours, 35 minutes. During endovascular thrombectomy (Figure 3, C), the embolus was partially debulked with aspiration techniques but proved challenging to traverse and only partial recanalization could be achieved (mTICI 2a). Pathology of the embolus revealed mature adipose tissue (Figure 3, D).

Delayed postprocedure CT of the head showed infarct burden (Figure 3, E). The procedure was complicated by small ICA dissection, incurred during attempts to cross the occlusion, without sequelae. NIHSS at 1 week was 5.

He was started on therapeutic anticoagulation and discharged to rehabilitation and eventually home. His mRS at 2 months was 2 (independent living but not back to the previous level of functioning).

DISCUSSION

We demonstrate that LVO is a relatively uncommon but potentially devastating complication after cardiothoracic surgery. The most important risk factors identified in our data were prolonged ACC times and CPB times. We also demonstrate a temporal trend, with evaluation and treatment greatest in the period after the presentation and publication of the trials supporting the positive treatment effect of mechanical thrombectomy (Video 1).

CTS is complicated by ischemic stroke in up to 3.1% of cases.^{7,8} Our series had an incidence of cerebrovascular complications post-CTS of 2.5%, with 92.5% ischemic strokes. In another large cohort of patients undergoing CTS, the incidence of stroke was similar to ours (2.6%). In that series, stroke incidence varied according to procedure type. Patients who had a stroke had a greater perioperative mortality rate and a longer period of hospitalization.⁹ Our study is the first to our knowledge to specifically report an LVO incidence post-CTS, which was 10.9% of ischemic strokes and 0.25% of all cardiothoracic procedures. Despite LVO ischemic stroke having a relatively low incidence in the general cardiothoracic patient population, these patients have a poor natural history.¹⁰

On univariate analysis, the only risk factor associated with LVO in our cohort was prolonged ACC times; this was even more significant in patients with EF >45%.

Prolonged ACC time has been reported in previous studies to be associated with a greater incidence of ischemic stroke post-CTS² and avoiding aortic crossclamping altogether (“no aortic touch” technique) is advocated as a means of stroke prevention.¹¹ Conversely, prolonged CPB time only became a significant risk factor in patients with EF >45%. In other studies, prolonged CPB times have been associated with increased risk of ischemic stroke; potential mechanisms include cerebral hypoperfusion and activation of coagulation and inflammatory cascades by contact with the extracorporeal bypass circuit.^{12,13} These latter mechanisms are likely important in the formation of macroemboli, which would predispose to LVO. Low EF is a known risk factor for ischemic stroke¹³; controlling for this likely accounted for a more robust association between ACC/CPB times and risk of LVO.

Also interesting is the greater incidence of LVO in patients with mechanical circulatory assist devices, although this did not reach statistical significance. Of note, the increased risk for microemboli with certain left ventricular assist devices has been previously reported using transcranial Doppler studies.¹⁴ Although most of these are asymptomatic, there is likely a greater risk of macroemboli as well, likely due to alteration in systemic immunologic and thrombostatic functions that have been documented as a result of direct contact between blood circulation and circulatory assist device materials.¹⁵ The lack of association between LVO and various preoperative vascular risk factors (in particular atrial fibrillation) may reflect that the vast majority of cerebrovascular events resulting in macroemboli in the setting of cardiothoracic surgery are due to direct endocardial and aortic manipulation.

Treatment of this patient population is unique in the treatment of LVO stroke. Intravenous tissue plasminogen activator is not an option due to recent surgery and therefore bleeding risk. Mechanical thrombectomy offers the best opportunity to reperfuse these patients. Of note, cardiothoracic patients were not included in the sentinel LVO stroke studies. Our retrospective study provides some of the first evidence of endovascular therapy results in this unique subgroup. This will hopefully help to decrease the significant gap that exists between evidence of treatment effect and treatment availability.

All patients treated with thrombectomy were treated after the publication of the 2015 stroke trials showing the benefit of endovascular intervention. This followed increased publicity around trial results, underscoring the importance of awareness about therapy, especially among non-neurologists. These patients are usually cared for in environments without dedicated neurologic expertise. In the absence of established protocols, long latencies to treatment are common (eg, long diagnosis to imaging times in our cohort, frequently due to delayed activation of the stroke team at the point of referral). We have since

formed a protocol incorporating a simple bedside assessment tool (G-FAST) to direct evaluation and management of future cases (see [Appendix E3](#)), with the goal of accelerating care.¹⁶

The logistics and workflow involved in stroke diagnostics for patients with LVO undergoing CTS may be challenging, compounded by potential additional invasive devices (eg, left ventricular assist devices) with which to travel to scan. Because of postoperative pacer wires and other surgical devices, this population is typically unable to undergo MR imaging, our preferred imaging modality for late-window stroke patient selection for intervention. We therefore use CT ASPECTS ([Appendix E1](#)) and collateral grading to evaluate established infarct core on CT/CTA in these patients, although this selection method is yet to be validated in late time windows.

For patients with deficit on emergence from anesthesia, LSW time could be anesthesia induction with loss of patient examination (which is what we use) or later, the moment of direct cardiac manipulation. Physiologically, it would be reasonable to expect stroke onset to coincide with cardiac manipulation or clamp placement/removal, as suggested by showers of microemboli seen by transcranial Doppler.¹⁷ Expectation for penumbral loss is unclear. Cerebral hypoperfusion and hypoxemia during bypass may produce ischemic pre- or per-conditioning.¹⁸ In addition, hypothermia may be protective for penumbral loss due to diminished tissue metabolic demand. These considerations in patients with LVO undergoing CTS remain to be studied.

The CTS subgroup of patients with LVO may develop unusual embolic pathology, compounding technical challenges associated with clot retrieval. One of our patients (case 5) had adipose tissue (likely epicardial) detected on pathologic examination of the embolus. Fat embolism is an uncommon but described mechanism of stroke after CTS.^{1,19} This patient demonstrated the hypodense arterial sign on non-contrast CT of the head in patients with fat embolism.²⁰ A second patient had suspected cardiac muscle embolus (pathology was not sent during the case). Unusual emboli interact with thrombectomy devices in unpredictable ways, increasing the risk of procedural complications and inadequate recanalization. Our longer median procedure time (43 minutes) and lower reperfusion rates reflect these technical challenges. Anticipating unusual emboli, we target direct aspiration (A Direct Aspiration First-Pass Technique) first in these cases.

Beyond thrombectomy itself, these patients present additional considerations during emergent stroke care. Vascular access may be challenged by virtue of common underlying cardiovascular and cerebrovascular risk factors such as peripheral arterial disease.⁷ Patients undergoing CTS have abnormal cerebral autoregulatory profiles²¹; this may have

TABLE 3. Cardiothoracic surgery and echocardiography data for LVO patients who underwent thrombectomy

Case	Cardiac surgery type	Echo findings	Aortic crossclamp time, min	Cardiac bypass time, min	Time from cardiac bypass onset/aortic crossclamp to stroke symptom detection	Additional procedure details
1	LVAD placement, TV repair	EF 13%; Moderate TR and severe MR, RV dilation, RVSP 44 mm Hg	—	130	7 h, 9 min/NA	HeartMate II implantable LVAD, TV repair. Partial ascending aorta clamp placed; no cardioplegic arrest.
2	Aortic valve replacement and arch repair for aneurysm	EF 72%, ascending aorta dilation, AR	81	146	11 h, 9 min/11 h, 11 min	Aorta transected 1.5 cm prox to crossclamp and taken all way down to sinotubular junction; valve excised and noted to be bicuspid and have calcified leaflets/annulus. St Jude's mechanical bioprosthesis placed. 24-mm HEMASHIELD graft anastomosed to supracoronary aorta supported by Teflon felt. Deep hypothermic circulatory arrest time 16 min.
3	Elective TAVR (at an outside hospital)	EF 70%; prosthetic valve	—	—	—	Performed at outside hospital; no intraoperative details available.
4	Previous BiVAD placement	EF 32%	—	77	39 d	Impella LVAD removed; partial aortic clamp placed; LVAD and RVAD CentriMag circuits placed.
5	Mitral valve replacement, maze	EF 65%; mobile density mitral valve, flail anterior leaflet.	125	176	15 h, 7 min/15 h, 34 min	Repair mitral valve, isolation pulmonary vein, left atrial appendage resection, left maze procedure.
6	Previous LVAD placement, previous CABG	EF 25%; LA dilation, aortic dilation, LV apical aneurysm; mitral valve prolapse	—	82	31 d	Revision of sternotomy ×2; insertion of LVAD (HeartWare)—no cardioplegic arrest.
7	CABG, contralateral CEA	42%	100	109	2 d	CABG ×5; mitral valve repair; contralateral carotid endarterectomy.

LVAD, Left ventricular assist device; TV, tricuspid valve; EF, ejection fraction; TR, tricuspid regurgitation; MR, mitral regurgitation; RV, right ventricle; RVSP, right ventricular systolic pressure; NA, not available; AR, aortic regurgitation; TAVR, transcatheter aortic valve replacement; BiVAD, biventricular assist device; RVAD, right ventricular assist device; LA, left atrium; LV, left ventricle; CABG, coronary artery bypass graft; CEA, carotid endarterectomy.

FIGURE 2. Images for case 1. A, Scout image showing pacemaker, endotracheal tube, sternal wires, and postoperative monitors. Patients are complex to move emergently for imaging evaluation and usually cannot undergo magnetic resonance imaging. B, Computed tomography angiography with right middle cerebral artery M1 cutoff and reasonable collaterals. C, Initial angiogram with proximal right M1 cutoff. D, Full recanalization after 3 passes. E, Day 2 computed tomography of the head showing final stroke volume.

implications for optimal blood pressure management during and after stroke intervention. These alterations may predispose to a greater hemorrhagic conversion risk in these patients, compounded by systemic anticoagulation and altered cerebrovascular flow dynamics—4 of 7 patients in our cohort had some evidence of hemorrhage on follow-up imaging; however, only 1 had clinically symptomatic hemorrhage.

This is the largest consecutive series of such patients to date. However, our study is subject to several limitations beyond the typical limitations of a retrospective single-center effort. Our database only collected data on neurologic complications until 30 days postprocedure (the period of greatest risk); later strokes could therefore have been missed. CTA/MR angiography imaging to diagnose LVO was not available in all patients. Therefore, the true LVO incidence might be slightly greater than what our findings report. Improved awareness and protocols may present

greater treatment opportunity than what we report. Finally, the risk of LVO depends in part on the nature of surgery performed and our academic medical center environment might not generalize to the CTS population at large.

CONCLUSIONS

LVO after CTS is an uncommon but potentially devastating complication. The most important risk factors identified were prolonged ACC and CPB times. Emergent revascularization with mechanical thrombectomy carries unique considerations in this population but resulted in improved stroke scores and a trend towards better functional outcomes at 3 months. Although larger prospective studies will be required to corroborate these findings, awareness among cardiac care providers of this therapeutic option for stroke patients in both early and late time windows is essential to ensure timely mobilization of endovascular stroke treatment teams.

FIGURE 3. Images for case 5. A, Initial CT of the head showing hypodensity in distal right M1. B, Corresponding vessel occlusion on CT angiography. C, Angiographic appearance of right M1 filling defect. Only a modified Thrombolysis in Cerebral Infarction 2a* result was achieved after both aspiration and stentriever attempts. D, Pathology on embolic fragments showing mature adipose tissue. E, Day 3 CT of head showing final infarct burden. *See Appendix E1.

Conflict of Interest Statement

Dr Hirsch reports personal fees from Medtronic and Data Safety and Monitoring Board service Cordis Neurovascular

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VIDEO 1. Brief video with summary of key findings and providing context for study by lead authors. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)33256-2/fulltext](https://www.jtcvs.org/article/S0022-5223(18)33256-2/fulltext).

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Key Words: cardiothoracic surgery, large-vessel occlusion, endovascular therapy, ischemic stroke

APPENDIX E1. RELEVANT CLASSIFICATION AND SCORING SYSTEMS IN COMMON USE IN STROKE CARE AND TRIALS

ASPECTS (Alberta Stroke Program Early CT Score):

Used for assessment of established infarct core in stroke patients. Infarcted tissue appears hypodense on computed tomography (CT), with loss of gray–white differentiation. A noncontrast CT scoring system (ranging from 0 to 10, 10 is normal) for hypodensities in different superficial and deep territories reflects the extent of early ischemic changes. Lower scores are associated with larger territory affected by ischemia. The larger the affected territory, the lower the chance that a patient will make a functional recovery.^{E1}

Hemorrhagic Transformation Grading Score

Hemorrhage after reperfusion is a feared complication. Determination is made on 24-hour CT or postprocedure CT. All hemorrhages are divided based on ECASS (European Cooperative Acute Stroke Study) criteria into 1 of the following subtypes outlined to follow:

- i. Hemorrhagic infarction type 1 (HI1): small hyperdense petechiae in the infarct bed with no mass effect;
- ii. HI2: more confluent hyperdensity throughout the infarct zone without mass effect;
- iii. PH1: homogeneous hyperdensity occupying less than 30% of the infarct zone, with some mass effect; and
- iv. Parenchymal hematoma type 2 (PH2): homogeneous hyperdensity occupying over 30% of the infarct zone, with significant mass effect.

This determination is important because of the implications for outcome. Patients with PH2 have a worsened 90-day outcome as a result of the hemorrhage, and are therefore the most compromised.^{E2}

NIHSS (National Institute of Health Stroke Scale)

A 15-item scale ranging from 0 to 42 that allows for an assessment of stroke-related neurologic deficits. Greater scores reflect more profound deficits and are more predictive of large-vessel occlusion (LVO). Most patients with LVO present with NIHSS >6, often >10.^{E3}

mRS (Modified Rankin Scale)

Disability rating score ranging from 0 (normal and intact neurologic function with no limitations) to 6 (death). Used in all major stroke trials as a measure of clinical/functional outcome. By convention, outcome is assessed at 90 days after stroke onset. Scores of 0 to 2 indicate patients have returned to functional independence, the ultimate goal of acute stroke therapy.^{E4}

mTICI (Modified Thrombolysis in Cerebral Ischemia) Score

Score that reflects extent of cerebrovascular reperfusion after mechanical thrombectomy. Greater degrees of reperfusion are associated with better patient

outcomes. The goal of endovascular therapy is to achieve at least 50% reperfusion of the threatened downstream ischemic territory. The modified score is summarized to follow:

Grade 0: no perfusion;

Grade 1: Antegrade reperfusion past the initial occlusion but limited distal branch filling with little or slow distal reperfusion;

Grade 2a: Antegrade reperfusion of less than half of the occluded target artery previously ischemic territory (eg, in 1 major division of the middle cerebral artery and its territory);

Grade 2b: Antegrade reperfusion of more than 50% of the previously occluded target artery ischemic territory (eg in 2 major divisions of the MCA and their territories); and

Grade 3: Complete antegrade reperfusion of the previously occluded target artery ischemic territory, with absence of visualized occlusion in all distal branches.^{E5}

APPENDIX E2. INSTITUTIONAL CARDIOTHORACIC INTENSIVE CARE UNIT LARGE VESSEL OCCLUSION STROKE PROTOCOL

Massachusetts General Hospital

Cardio-Thoracic Surgery Large Vessel Occlusion Stroke Protocol

A collaboration between Cardiothoracic Surgery, the Heart Center ICU, Stroke and Neuroendovascular Surgery

Aim:

To provide a standardized institutional approach to cardiac surgery patients with post-operative deficit that may be caused by large-vessel occlusion (LVO).

Background:

Stroke from LVO is a major complication after surgery involving the heart and aortic arch. The new data showing the powerful therapeutic impact of endovascular therapy (thrombectomy) for patients with LVO means there is now a therapy for these patients. This data extends to 24 hours from last known well, but is likely true into even later timeframes.

Process:

Preoperatively

High-risk patient identified (left ventricular access, extracorporeal devices, arch repairs, valve replacements, etc) preoperatively and anesthesia informed. Risk is determined by surgical service.

Consider continuous electroencephalography (EEG) monitoring during the case (including emergencies), looking for asymmetry upon rewarming as a marker of a new intracranial concern.

For patients at high risk of LVO:

High risk determination either due to perioperative characteristics or with EEG monitoring findings, as decided by the surgical team.

Order a STAT computed tomography angiography (CTA) of the head and neck with delays (Acute Stroke Imaging Protocol), obtain study in transporting the patient from the operating room (OR) to the heart center intensive care (ICU) unit while the patient is under the care of the anesthesia team. This is booked at the end of the case and radiology informed immediately before patient transport to the scanner to ensure the scanner is available.

Stroke on-call and neuroendovascular fellows are paged from the OR to mobilize to scanner to review findings.

For candidates with confirmed LVO who are candidates for mechanical thrombectomy, the patient is then transported by the anesthesia team directly to OR after the neuroendovascular fellow has emergently booked the case.

In the absence of LVO or an intervenable lesion, the patient proceeds to the heart center ICU as before.

For all other patients:

Postoperative protocol proceeds as usual (eg, patient is transferred to the cardiac unit, sedation is turned off when patient reaches a temperature of 36°).

Bedside nurse should evaluate patient during emergence from sedation, assessing for focal deficit. Specifically, look for any asymmetry of motor function, inability to follow simple commands and gaze preference. Apply scale (ie, G-FAST).

The heart center ICU team must be alerted immediately if deficit is identified. This is true irrespective of time from last known well.

Stroke on-call activation based on finding of focal neurologic deficit.

Establish last seen well time (anesthesia induction) and time of risk (eg, ventricular cannulation, aortic cross clamp time, etc). Therapy will be considered for up to 48 hours from last seen well, based on the imaging profile.

Order and transport patient for STAT computed tomography (CT)/CTA head and neck with delays (Acute Stroke Imaging Protocol). This order should happen simultaneously with the page to Stroke on-call. Stroke team will alert neuroendovascular team. Ideally, the patient will be met at the scanner by neuroendovascular and Stroke fellows.

If CTA confirms LVO (ICA, proximal middle cerebral artery branches, basilar) then case will be booked for emergent mechanical thrombectomy by the neuroendovascular fellow. (If not, stroke service will make further recommendations regarding management).

For LVO patients, proceed directly from CT scanner to OR for thrombectomy.

Post-thrombectomy disposition based on patient characteristics. Typically return to the heart center ICU with neuro ICU consult and vascular neurosurgery following, although rarely admission to the neuro ICU will be more appropriate.

Short-term postoperative imaging within 24 hours of procedure (likely portable CT, since many will have cardiac contraindications to magnetic resonance imaging, eg, pacing wires, left ventricular assist device, etc).

Data will be captured by the existing cardiothoracic surgery database to track rates and outcomes

APPENDIX E3. BEDSIDE STROKE EVALUATION PER INSTITUTIONAL CARDIOTHORACIC INTENSIVE CARE PROTOCOL

G-FAST

Gaze: forced eye deviation to the left or right

Face: Facial asymmetry

Arm: weakness of one arm, inability to lift off the bed

Speech: Slurred/unintelligible speech, inability to follow commands, or mutism

Each finding on examination is given a single point if present, and score is added. Greater scores are more predictive of LVO. (For a score of 3 approximately 1 of 5 of patients will have an LVO, for a score of 4 approximately 1 of 2 patients will.) This scale is one of several simplified and equivalent clinical scoring systems that allow rapid clinical evaluation at the bedside.^{E6}

E-References

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