Original article

Incidence of perioperative stroke in thoracic aortic surgical patients with deep hypothermic circulatory arrest

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Objective To identify the incidence of stroke, factors associated with stroke and the outcomes of patients undergoing thoracic aortic surgery with deep hypothermic circulatory arrest (DHCA)

Methods This retrospective study was conducted in 165 patients undergoing thoracic aortic surgery with DHCA from January 1, 2005 to December 31, 2013. The patients were identified as stroke, if there was a new event of neurological deficit that persisted for at least 24 hours after its onset; whether it was present after surgery, or developed after first emergence from anesthesia without a neurological deficit. Perioperative factors were reviewed for association with stroke, e.g. the American Society of Anesthesiologists (ASA), underlying diseases and main anesthetic techniques. Clinical status, and lengths of stay in the intensive care unit (ICU) and hospital were explored for patient outcomes.

Results Eighteen (11%) from 165 patients had perioperative stroke. Six factors from univariate analysis were significantly related to perioperative stroke, such as age >65 years, emergency cases and unstable hemodynamics on arrival at the operating room. However, no significant variable remained from multivariate analysis. The cross-clamp time was significantly longer among the group with stroke (p =0.046). The mortality rate was lower among stroke patients (6%) than no-stroke patients (10%), but not significantly different, p =0.529. The median lengths of ICU and hospital stays were significantly longer in the stroke group, when compared to the no-stroke group, p <0.001 and p <0.001, respectively.

Conclusions The incidence of perioperative stroke after thoracic aortic surgery with DHCA was 11%. Patients diagnosed as stroke stayed longer in the ICU and hospital than those without stroke
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keywords: perioperative stroke, thoracic aortic surgery, deep hypothermic circulatory arrest (DHCA)

Introduction

The deep hypothermic circulatory arrest (DHCA) technique, for use in profound systemic hypothermia, provides suitable surgical conditions, while decreasing the risk of organ ischaemia[1]. In spite of its advantages, DHCA requires a prolonged cardiopulmonary bypass (CPB), which has related problems of coagulopathy and cerebral microembolism. Both CPB and DHCA are related to factors that cause flow-metabolic uncoupling. Therefore,

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CPB followed by neurologic injury can result from hypoxic, ischemic, embolic, reperfusion, and inflammatory mechanisms[2,3].

There were no reviews or reports of perioperative stroke incidence in this university hospital. Thus, the objectives of this study were to identify the incidence, related factors of perioperative stroke and outcomes of patients undergoing thoracic aortic surgery with DHCA at a major teaching hospital in northern Thailand. This study should enable further development in this institute by providing useful data on guidelines for perioperative management in thoracic aortic surgery with DHCA.

Methods

After approval from the Institutional Review Board at the Faculty of Medicine, Chiang Mai University, the authors performed a retrospective study of patients undergoing thoracic aortic surgery with DHCA (cooling between 15-25 °C was accomplished over 30-60 minutes)[4] from January 1, 2005 to December 31, 2013. The exclusion criteria comprised a stroke history of within one month and condition of coma before surgery, and the medical records of 165 patients were reviewed for analysis. The primary aim of this study was to find the incidence of perioperative stroke, by adapting a published definition[5,6] as a new event of neurological deficit that persisted for at least 24 hours after its onset; whether it was present after surgery, or developed after first emergence from anesthesia without a neurological deficit. This was confirmed using abnormal imaging (CT of the brain) and diagnosed by a neurologist. The patients were then categorized according to whether they had been diagnosed as stroke or not.

The collected demographic and preoperative data included age, body mass index (BMI), sex, underlying diseases (e.g. hypertension, diabetes mellitus and renal dysfunction), and stability of hemodynamics on arrival at the operating room. Additional intraoperative factors were included and analyzed such as diagnosis and operation, anesthetic technique and its duration, cardiopulmonary bypass time (CPB) (including cross-clamp time, circulatory arrest time, and re-warming time), cerebral perfusion technique and time, lowest and highest core temperature, neuroprotective agents and the bispectral index (BIS) monitor used. Other reviewed data involved postoperative complications, clinical status and length of ICU and hospital stays.

The authors used SPSS version 20 to perform statistical analysis. The chi-square or Fisher's exact test was used for univariate analysis of factors associated with stroke and compared to those with no stroke. Variables with a univariate *p*-value <0.20 were entered for multivariate analysis using logistic regression to identify factors, with *p*-value <0.05 considered statistically significant.

Results

One hundred and sixty five patients had thoracic aortic surgery with DHCA, due to thoracic aortic dissection (58%) or thoracic aortic aneurysm (42%). Eighteen patients (11%) had perioperative stroke. The cause of stroke was diagnosed as cerebral emboli and ischemia in 56% and 44% of the cases, respectively. Six factors from univariate analysis were related significantly to perioperative stroke, with a $p <0.20$. However, no significant variable remained upon multivariate analysis (Table 1).

There was no significant difference between the stroke and no-stroke group in anesthetic time, cardiopulmonary bypass time, circulatory arrest time, or cerebral perfusion time and technique. Only the cross-clamp time was significantly longer among stroke patients (p = 0.046) (Table 2).

Patients in the stroke group (with normal or impaired consciousness) were more dependent on a ventilator than those in the no-stroke group at 72 hours and 1 week post operation. There was no evidence of brain pathology from CT brain imaging in the no-stroke group, as confirmed by a neurologist. Perhaps these patients were in an unstable hemodynamic condition, and required inotropic or vasopressor support. The median lengths of ICU and hospital stays were significantly longer in the stroke group, when compared to those in the no-stroke group, $p <0.001$ and $p <0.001$, respectively. The mortality rate was lower among stroke patients, (1, 6%) than that in the no-stroke group (15, 10%), but with no significant difference, p =0.529. The one patient in the stroke group died of septic shock, whereas 3, 4 and 8 patients in the no-stroke group died due to massive hemorrhage, septic shock and cardiogenic shock, respectively. All the deaths occurred postoperatively.

Table 1. Univariate and multivariate analyses of factors associated with stroke versus no stroke (See footnotes for other abbreviations used.)

Factor	Stroke No(%) (n=18)	No stroke No(%) (n=147)	Univariate analysis (Crude OR) OR (95%CI)	*p**	Multivariate analysis (Adjusted OR) OR (95%CI)	*p***
Age						
<65 years	10 (56%)	40 (27%)	3.34	**0.014†**	2.99	0.058
≥65 years	8 (44%)	107 (73%)	(1.23-9.07)		(0.96-9.26)	
Sex:						
Male	11 (61%)	89 (61%)	1.02	0.963†		
Female	7 (39%)	58 (39%)	(0.38-2.79)			
ASA						
IV-V	7 (39%)	26 (18%)	2.96	0.055‡		
II-III	11 (61%)	121 (82%)	(1.05-8.36)			
Emergency						
Yes	9 (50%)	36 (25%)	3.08	**0.045‡**	0.37	0.169
No	9 (50%)	111 (75%)	(1.14-8.36)		(0.09-1.52)	
Hemodynamic at operating room arrival§						
Unstable	2 (11%)	0 (0%)	10.19	**0.011‡**	0.00	
Stable	16 (89%)	147 (100%)	(6.40-16.22)		(0.00)	
Previous myocardial ischemia						
Yes	0 (0%)	8 (5%)	1.13	0.600‡		
No	18 (100%)	139 (95%)	(1.07-1.20)			
Atrial fibrillation						
Yes	1 (6%)	4 (3%)	2.10	0.443‡		
No	17 (94%)	143 (97%)	(0.22-19.92)			
Hypertension						
Yes	13 (72%)	81 (55%)	2.12	**0.166†**	0.63	
No	5 (28%)	66 (45%)	(0.72-6.25)		(0.18-2.27)	
Dyslipidemia						
Yes	5 (28%)	20 (14%)	2.44	**0.156‡**	0.48	
No	13 (72%)	127 (86%)	(0.79-7.59)		(0.12-1.99)	
Diabetes mellitus						
Yes	3 (17%)	7 (5%)	4.00	**0.081‡**	0.57	
No	15 (83%)	140 (95%)	(0.94-17.11)		(0.09-3.44)	
COPD						
Yes	1 (6%)	10 (7%)	0.801	1.000‡		
No	17 (94%)	137 (93%)	(0.09-6.69)			
Renal dysfunction						
Yes	7 (39%)	38 (26%)	1.83	0.267‡		
No	11 (61%)	109 (74%)	(0.66-5.05)			
Main anestheitc agent						
TIVA	1 (5%)	18 (12%)	0.333†			
Sevofluranne	16 (90%)	107 (73%)				
Isoflurane	1 (5%)	22 (15%)				
Cerebral perfusion technique						
No	3 (16%)	27 (18%)	0.253†			
ACP	13 (72%)	116 (79%)				
RCP	1 (6%)	1 (1%)				
Both	1 (6%)	3 (2%)				

Table 1. (Continue)

Factor	Stroke No(%) (n=18)	No stroke No(%) (n=147)	Univariate analysis (Crude OR)		Multivariate analysis (Adjusted OR)	
			OR (95%CI)	*p**	OR (95%CI)	*p***
Neuro protective agent						
No	13 (72%)	89 (60%)		0.789†		
Dexamethasone	3 (16%)	39 (27%)				
Thiopental	1 (6%)	11 (8%)				
Both	1 (6%)	8 (5%)				
BIS monitor						
No	15 (83%)	131 (89%)	0.61	0.440‡		
Yes	3 (17%)	16 (11%)	(0.16-2.34)			
Vasopressor during off CPB						
Yes	16 (89%)	130 (89%)	0.99	1.000‡		
No	2 (11%)	16 (11%)	(0.21-4.68)			

Abbreviations:
ACP, antegrade cerebral perfusion; ASA, American Society of Anesthesiologists; BIS, Bispectral index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; OR, odds ratio; RCP, retrograde cerebral perfusion; TIVA, total intravenous anesthesia
* p <0.20 considered significant, and are **boldfaced**; **p <0.05 considered significant, and are **boldfaced**
† Chi-square test; ‡ Fisher's exact test,
§ Stable = Blood pressure ≥ 90/60 mm.Hg. without inotropic or vasopressor drugs

Table 2. Intraoperative data

Data*	Stroke (n=18)	No stroke (n=147)	*p***
Anesthetic time (min)	375 (315-409)	360 (300-425)	0.965
CPB time (min)	215 (161-230)	185 (156-225)	0.439
Cross clamp time (min)	124 (90-152)	91 (64-138)	**0.046†**
Circulatory arrest time (min)	36 (25-54)	27 (17-47)	0.250
Cerebral perfusion time (min)	36 (22.2-53.2)	24 (10-56)	0.265
Rewarm time (min)	65 (54-90)	60 (45-75)	0.213
Lowest esophageal T (°C)	22.0 (19.5-25.8)	22.0 (18.0-25.0)	0.665
Highest esophageal T (°C)	36.3 (35.6-37.1)	36.8 (36.1-37.3)	0.206

Abbreviations: °C, Celsius degree; CI, confidence interval; CPB, cardiopulmonary bypass; IQR, Interquartile range; min, minute; OR, odds ratio; T, temperature
* values presented as median [IQR];
**Unless stated otherwise, values determined by Mann–Whitney U-test
† p-values < 0.05 considered significant, and are boldfaced.

Discussion

The incidence of perioperative stroke after thoracic aortic surgery with DHCA was 11% in this institute. Acute neurologic injury related to CPB can result from several causes, e.g. hypoxic, ischemic, embolic, reperfusion, and inflammatory mechanisms[2,3]. Previous literature reported that the incidence of stroke varied between 3.8-11% in patients undergoing thoracic surgery with DHCA[7–10]. Causes of stroke were reported from the time of stroke onset, however, the mechanism seemed not different in either early or delayed onsets. Similar to the results of this study, embolism was the

Table 3. Postoperative clinical outcome

Outcome	Stroke [No (%)] (n=18)	No stroke [No (%)] (n=147)	*p**
Reoperation			
No	18 (100%)	127 (87%)	0.095
Stop bleeding	0 (0%)	18 (12%)	0.116
Redo-surgery	0 (0%)	2 (1%)	0.617
Cardiac arrest			
Yes	2 (11%)	11 (8%)	0.589
No	16 (89%)	136 (92%)	0.589
Postoperative status at 72 hours			
Normal consciousness	1 (6%)	119 (81%)	**0.000†**
Normal consciousness with ventilator support	6 (33%)	13 (9%)	**0.002†**
Impaired consciousness with ventilator support	11 (61%)	9 (6%)§	**0.000†**
Death	0 (0%)	6 (4%)	0.384
Postoperative status at 1 week			
Normal consciousness	6 (33%)	123 (84%)	**0.000†**
Normal consciousness with ventilator support	7 (39%)	10 (7%)	**0.000†**
Impaired consciousness with ventilator support	4 (22%)	5 (3%)§	**<0.001†**
Death	1 (6%)	9 (6%)	0.920
Discharge status			
Alive	17 (94%)	132 (90%)	0.529
Death	1 (6%)	15 (10%)	0.529
Time to awake (hour): (median [IQR])	4 (3-8)	4 (2-6)	0.177‡
ICU stay (day): (median [IQR])	8 (5-13)	3 (2-4)	**<0.001‡**
Hospital stay (day): (median [IQR])	16 (11-37)	7 (6-11)	**<0.001‡**

Abbreviations:
CI, confidence interval; ICU, intensive care unit; IQR, Interquartile range; OR, odds ratio
* Unless stated otherwise, values determined by chi-square test of proportion (Z test)
† *p* <0.05 considered significant, and are boldfaced; ‡ Mann–Whitney U-test;
§ there was no evidence of brain pathology in CT brain imaging, confirmed by the neurologist

major cause of stroke, followed by cerebral hypoperfusion[11].

Appoo, *et al*[10] reported that prior sternotomy, previous stroke, atrial fibrillation, and chronic obstructive pulmonary disease were factors associated with perioperative stroke. Conolly, *et al*[1] found that increased age, longer length of DHCA, and atheroma or thrombus were the predictors of stroke after DHCA. Duration of DHCA also was reported as a risk factor of decreased cerebral oxygen delivery in addition to anemia, hypocarbia, alkalosis and lower flow rates[12]. Although the DHCA duration in this study was not prolonged significantly in stroke patients, cross-clamp time was longer in those who had perioperative stroke, as mentioned by Stamou, *et al*[13] Perhaps the number of thoracic surgical patients with DHCA in that study was so small that a possible stroke factor could not be found by this one.

The durations of ICU and hospital stays were significantly longer among stroke patients[10,13], and were similar to those in this study. However, the incidence of hospital mortality was no higher in this study at 6% and 10% in stroke and no-stroke patients, respectively, whereas other studies reported a varied stroke mortality rate of between 14.4% and 33%[10,13].

In addition to the small sample size, there were other limitations in this study. Firstly, it was a retrospective study, and therefore some data were missing. Furthermore, no routine preoperative carotid ultrasound was performed to detect the presence and severity of carotid stenosis. In addition, intraoperative cerebral blood flow monitoring, e.g. transcranial Doppler ultrasound, electroencephalography (EEG) and near infrared spectroscopy (NIRS) was not available for helping with the early detection of perioperative stroke. Lastly, there was no standard guideline in the management of cerebral protection during thoracic aortic surgery with DHCA.

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Conflicts of interest

None

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อุบัติการณ์โรคหลอดเลือดสมองในผู้ป่วยที่มารับการผ่าตัดหลอดเลือดเอออร์ตาระดับทรวงอก ที่ใช้เทคนิค deep hypothermic circulatory arrest

อานันท์ชนก ศฤงคารินกุล, และ กิตติคุณ จอมใจ
ภาควิชาวิสัญญีวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

วัตถุประสงค์ เพื่อหาอุบัติการณ์ ปัจจัยที่เกี่ยวข้องกับการเกิดโรคหลอดเลือดสมอง (stroke) และผลการรักษาในผู้ป่วยที่มารับการผ่าตัดหลอดเลือดเอออร์ตาระดับทรวงอกที่ใช้เทคนิค deep hypothermic circulatory arrest (DHCA)

วิธีการศึกษา เป็นการศึกษาแบบย้อนหลัง โดยเก็บข้อมูลจากผู้ป่วยทั้งหมด 165 ราย ที่มารับการผ่าตัดหลอดเลือดเอออร์ตาระดับทรวงอกที่ใช้เทคนิค DHCA ในช่วงเดือนมกราคม พ.ศ. 2548 ถึงเดือนธันวาคม พ.ศ. 2556 กลุ่มที่เกิด stroke คือ ผู้ป่วยที่มีอาการผิดปกติทางระบบประสาทนานมากกว่า 24 ชั่วโมงหลังจากเริ่มมีอาการแสดง โดยอาจตรวจพบหลังการผ่าตัด หรือเกิดขึ้นหลังจากที่ผู้ป่วยฟื้นจากภาวะสลบโดยไม่มีความผิดปกติทางระบบประสาท แต่มีอาการแสดงภายหลังจากนั้น ปัจจัยที่เกี่ยวข้องกับผู้ป่วยในระหว่างผ่าตัด ได้ถูกนำมาทบทวนถึงความสัมพันธ์ กับการเกิด stroke ได้แก่ American Society of Anesthesiologists (ASA) โรคประจำตัว และเทคนิคการระงับความรู้สึก ด้านผลของการรักษาได้พิจารณาจากอาการทางคลินิก ระยะเวลาการอยู่ในหอผู้ป่วยหนักและระยะเวลาการอยู่ในโรงพยาบาลของผู้ป่วย

ผลการศึกษา มีผู้ป่วยเกิด stroke ระหว่างผ่าตัด 18 ราย โดยคิดเป็นร้อยละ 11 จากผู้ป่วยทั้งหมด 165 ราย ผลการวิเคราะห์แบบ univariate analysis พบว่ามี 6 ปัจจัยที่สัมพันธ์กับการเกิด stroke อย่างมีนัยสำคัญ ได้แก่ อายุมากกว่า 65 ปี ผู้ป่วยรับการผ่าตัดฉุกเฉิน และผู้ป่วยที่สัญญาณชีพไม่คงที่ขณะมาถึงห้องผ่าตัด แต่จากการวิเคราะห์แบบ multivariate analysis ไม่พบว่ามีปัจจัยใดที่สัมพันธ์กับการเกิด stroke ในระหว่างผ่าตัดอย่างมีนัยสำคัญ ผลการศึกษาพบว่าระยะเวลา cross-clamp หลอดเลือดแดงเอออร์ตายาวนานกว่าอย่างมีนัยสำคัญในกลุ่มที่เกิด stroke (p = 0.046) อัตราการตายของผู้ป่วยในกลุ่มที่เกิด stroke (ร้อยละ 6) น้อยกว่ากลุ่มที่ไม่เกิด stroke (ร้อยละ 10) แต่ไม่มีความแตกต่างกันอย่างมีนัยสำคัญ (p =0.529) ระยะเวลาการอยู่ในหอผู้ป่วยหนัก และในโรงพยาบาลในกลุ่มที่เกิด stroke ยาวนานกว่ากลุ่มที่ไม่เกิด stroke โดย $p <$ 0.001 และ $p <$0.001 ตามลำดับ

สรุปผลการศึกษา อุบัติการณ์การเกิด stroke ระหว่างผ่าตัดในผู้ป่วยที่มารับการผ่าตัด หลอดเลือดเอออร์ตาระดับทรวงอกที่ใช้เทคนิค DHCA คิดเป็นร้อยละ 11 และผู้ป่วยที่ได้รับการวินิจฉัย stroke มีระยะเวลาการอยู่ในหอผู้ป่วยหนัก และในโรงพยาบาลนานกว่า **เชียงใหม่เวชสาร 2558;54(2):89-95.**

คำสำคัญ: โรคหลอดเลือดสมอง การผ่าตัดหลอดเลือดเอออร์ตาระดับทรวงอก