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Hypothermic Circulatory Arrest for Cerebral Protection During Combined Carotid and Cardiac Surgery in Patients with Bilateral Carotid Artery Disease

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Objective

The authors evaluated the protective effect of hypothermic circulatory arrest for patients with bilateral carotid artery disease who underwent cardiac surgical procedures.

Summary Background Data

Severe bilateral carotid artery disease coexisting with cardiac disease that requires surgical treatment is associated with a substantial incidence of stroke after operations that require cardiopulmonary bypass. The optimal method of management of patients with these coexisting conditions is not established clearly. Because hypothermia has a protective effect on neural and myocardial tissue during cardiac operations, a protocol employing profound hypothermia and a period of circulatory arrest was evaluated in a group of patients who underwent combined carotid and cardiac surgery who were considered to be at increased risk for the development of stroke.

Methods

Fifty patients with bilateral carotid artery disease, including 24 patients with high-grade unilateral stenosis and contralateral occlusion and 6 patients with 80% to 99% bilateral stenosis, underwent combined carotid endarterectomy and cardiac surgery (coronary artery bypass grafting in all 50 patients and additional procedures in 8 patients). Profound systemic hypothermia (15 C) was instituted, and the carotid endarterectomy was performed during a period of circulatory arrest that averaged 30 minutes. The cardiac procedure was performed during the periods of cooling and rewarming.

Results

The 30-day mortality rate was 6% (3 patients). There were no early postoperative strokes or reversible ischemic neurologic deficits. There have been seven late deaths in the postoperative period, which extends to 54 months. None of these deaths were caused by stroke. There has been one late stroke, which occurred in the distribution of the unoperated carotid artery.

Conclusions

This technique provides adequate protection of the brain and myocardium during combined carotid and cardiac surgical procedures and appears to reduce the frequency of stroke in the high-risk subgroup of patients with bilateral carotid artery disease.

The optimal management of patients with coexisting cardiac and carotid artery disease who require cardiac surgical procedures (most commonly coronary artery bypass grafting) remains unclear. The presence of carotid artery occlusive disease, particularly if it is bilateral, is a risk factor for the development of neurologic injury following cardiac operations.[1-7] It also is associated with a higher operative mortality rate after cardiac surgery than that observed after cardiac operations in patients without carotid artery disease.[1-7]

Studies in which large numbers of patients who underwent cardiac operations were screened preoperatively for the presence of carotid artery disease, using oculoplethysmography, carotid duplex scanning, and angiography, have shown that the presence of bilateral carotid artery disease is associated with a substantial incidence of neurologic ischemic events (approximately 10%), regardless of whether carotid endarterectomy was performed at the time of the cardiac operation.[3,5-7] This is particularly true for patients who have occlusion of one internal carotid artery and a significant stenosis of the other, in which ischemic event rates as high as 15% to 33% have been reported.[2,8] Because hypothermia has a protective effect on neural tissue during operations on the heart and thoracic aorta, as well as on the myocardium, we evaluated a protocol that employed profound systemic hypothermia and a period of hypothermic circulatory arrest to perform combined carotid endarterectomy and cardiac surgical procedures in patients with significant (>50% stenosis) bilateral carotid artery disease who were considered to be at increased risk for the development of stroke in the early postoperative period.

PATIENTS AND METHODS

Between April 1989 and September 1993, 50 patients with bilateral carotid artery disease and cardiac disease requiring operation underwent combined carotid endarterectomy and cardiac surgery using a technique that employed profound systemic hypothermia, a period of circulatory arrest during which the carotid endarterectomy was performed, and use of cold blood cardioplegia for myocardial protection. During the same interval, 19 patients with unilateral carotid artery disease who had combined carotid endarterectomy and cardiac surgery had the procedures performed using other techniques. The mean age of the 50 patients was 68 years (range = 49–82 years), and 36 (72%) were men.

Table 1. SEVERITY OF BILATERAL CAROTID ARTERY DISEASE DETECTED BY DUPLEX SCANNING IN THE 50 PATIENTS

Percent Stenosis	No. of Patients
100/80-99	13
100/50-79	11
80-99/80-99	6
80-99/50-79	15
50-79/50-79	5
Total	50

Preoperative Evaluation

Carotid Artery Disease

During the study interval, patients 65 years of age or older who had cardiac operations underwent routine preoperative duplex scanning of the carotid arteries.[6] Younger patients with symptoms suggestive of transient ischemic attacks or amaurosis fugax or with a history of stroke also had duplex scanning. The severity of the bilateral carotid artery disease identified in the 50 patients is shown in Table 1. Twenty-four of the patients (48%) had total occlusion of one internal carotid artery and significant (>50%) stenosis of the other. An additional six patients (12%) had severe (80% to 99%) stenosis of both internal carotid arteries. Thirteen patients had histories of stroke, and five patients had histories of transient ischemic attacks or amaurosis fugax. Thus, the bilateral carotid artery disease was identified in 64% of the patients only because they underwent preoperative duplex scanning. The scan findings were confirmed by carotid arteriography or magnetic resonance flow imaging in 32 of the 50 patients. In the remaining 18 patients, the decision to perform the carotid endarterectomy was based on the duplex study alone.[9] In the asymptomatic patients with equally severe disease bilaterally, the endarterec-

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Table 2. PREOPERATIVE CHARACTERISTICS OF THE 50 PATIENTS

Characteristic	No. of Patients	Percent
Male gender	36	72
Hypertension	35	70
Diabetes	16	32
Peripheral vascular disease	17	34
Smoking history	33	66
Stroke	13	26
TIA or amaurosis fugax	5	10
Previous cardiac surgery	4	8

* TIA = transient ischemic attack.

tomy was performed on the artery that supplied the dominant cerebral hemisphere.

Cardiac Disease

All patients had coronary artery disease and underwent coronary artery bypass grafting. The prevalence of risk factors for atherosclerosis and other preoperative variables, using criteria described previously,[10] are shown in Table 2. The severity of coronary artery disease and left ventricular dysfunction are shown in Table 3. Thirty-two patients (64%) had an unstable anginal syndrome.[11] All patients had multivessel coronary artery disease. Left main coronary artery stenosis (>50%) was present in 21 (42%) of the 50 patients. Five patients required urgent operation within the first 24 hours after cardiac catheterization. An intra-aortic balloon was inserted preoperatively in one patient. Four patients had valvular disease, which required valve replacement (two aortic, two mitral). Severe ascending aortic atherosclerosis was detected intraoperatively by epi-aortic ultrasonic imaging in four patients who had resection and graft replacement of the ascending aorta and proximal aortic arch in addition to coronary artery bypass grafting and carotid endarterectomy.[12]

Operative Technique

The carotid artery was exposed through an oblique incision in the neck and a segment of saphenous vein was excised simultaneously from a lower extremity. A median sternotomy incision then was made, one or both internal mammary arteries were mobilized, and the pericardium was divided. Systemic cooling was initiated immediately after establishing cardiopulmonary bypass. The ascending aorta was clamped and a cold (4 C), blood cardioplegic solution was infused into the aortic root for 2 minutes, at a rate of 250 to 300 mL/min. Additional cardioplegic solution was infused retrogradely through a balloon-tipped catheter, which was placed into the coronary sinus for 2 to 3 minutes, at a rate of 150 to 250 mL/min. Subsequent infusions of cardioplegic solution were infused through the coronary sinus at 20- to 25-minute intervals during the period of aortic clamping. The myocardial temperature was measured in the anterior ventricular septum and was maintained between 12 C and 15 C during the period of aortic clamping.

During the period of systemic cooling, a part of the cardiac surgical procedure was performed. This consisted of isolated coronary artery bypass grafting in 42 patients and coronary artery bypass grafting combined with valve replacement or resection and graft replacement of a severely atherosclerotic ascending aorta in 8 patients. (Table 3). When the nasopharyngeal temperature reached 12 C to 15 C (mean = 13.4 C ± 1.5 C) and the bladder or rectal temperature reached 15 C to 24 C (mean = 17.6 C ± 3.3 C), circulatory arrest was established. Clamps were placed on the common, internal, and external carotid arteries to prevent the introduction of air into the cerebral circulation. The carotid endarterectomy was performed through a longitudinal incision,

Table 3. PREOPERATIVE AND OPERATIVE CARDIAC-RELATED VARIABLES IN THE 50 PATIENTS

Variable	No. of Patients	Percent
New York Heart Association Class		
I	0	
II	10	20
III	16	32
IV	24	48
Unstable angina	32	64
Extent of coronary artery disease		
One vessel	0	0
Two vessel	5	10
Three vessel	24	48
Left main	21	42
Left ventricular wall motion score (CASS) (mean = 10)		
5	10	20
6–10	17	34
11–15	18	36
≥16	5	10
Urgent operation	5	10
Combined CABG, CEA and valve replacement	4	8
Combined CABG, CEA and resection of ascending aorta	4	8

CASS = coronary artery surgery study; CABG = coronary artery bypass grafting; CEA = carotid endarterectomy.

Table 4. INTRAOPERATIVE VARIABLES IN THE 50 PATIENTS

Operative Period	Duration	
	Mean ± SD (min)	Range (min)
Cooling	51 ± 12	28–85
Circulatory arrest	30 ± 8.7	14–60
Rewarming	81 ± 2	27–164
Cardiopulmonary bypass	134 ± 25	74–191

which was closed with a patch of saphenous vein. Low flow was established just before closure of the arteriotomy, and air was evacuated from the carotid bulb by temporarily removing the clamp on the internal carotid artery. Antegrade flow then was established by removing the clamps on the common and the external carotid arteries while temporarily occluding the internal carotid artery. Rewarming of the patient then was initiated.

The remainder of the cardiac procedure was completed during the period of rewarming. In the four patients who required replacement of the ascending aorta and the proximal aortic arch, a second period of hypothermic circulatory arrest was established after perfusing the brain for 5 minutes after the initial period of circulatory arrest. The ascending aorta and arch were replaced with a woven Dacron graft, and the saphenous vein bypass grafts were sutured to the graft. In all cases, when the rectal/bladder temperature reached 34 C, cardiopulmonary bypass was discontinued. The heart was decannulated, hemostasis was obtained, and the chest incision was closed after placement of chest drainage catheters. The neck incision was closed over a small drainage catheter that was attached to suction. The durations of cooling, circulatory arrest, rewarming, and cardiopulmonary bypass are shown in Table 4.

RESULTS

Early

Mortality

The 30-day mortality rate was 6% (3 patients). One patient died of shock on the second postoperative day. This resulted from extensive infarction of the small bowel, which was likely present preoperatively. This patient required urgent operation because of an unstable anginal syndrome. One patient died of a ventricular arrhythmia on the ninth postoperative day, and one patient died of respiratory failure on the twenty-ninth postoperative day. All three patients were awake in the early postoperative period and had no neurologic deficits.

Morbidity

There were no postoperative strokes or reversible ischemic neurologic deficits. One patient required reoperation for bleeding. Seven patients required intra-aortic balloon pumping in the postoperative period. Six patients required mechanical ventilation for more than 48 hours. Thirty-three patients (66%) were extubated postoperatively within the first 24 hours. The median length of stay in the intensive care unit was 3 days. Twenty-three patients remained in the intensive care unit for less than 48 hours. The median postoperative length of stay was 8.5 days. Thirty-four patients (68%) were discharged by the tenth postoperative day.

Late

Follow-up information was available for all 47 30-day survivors and extends to 54 months (mean = 14 months). There have been seven late deaths. Two of these deaths were sudden and occurred 2 and 3 months postoperatively. They were presumed to be of cardiac origin. Two deaths resulted from sepsis 2 and 37 months postoperatively, and three resulted from renal failure 14, 23, and 32 months postoperatively. There was one late stroke, which occurred 16 months postoperatively. This occurred in the distribution of the unoperated carotid artery, which had an 80% stenosis at the time of operation, as determined by duplex scanning. One patient sustained a transient ischemic attack 1 month postoperatively, which occurred in the distribution of the carotid artery that was totally occluded preoperatively by duplex scanning and magnetic resonance angiography. Two patients underwent subsequent endarterectomies of the other carotid artery.

DISCUSSION

The optimal management of patients with severe carotid artery disease requiring cardiac surgical procedures remains controversial. Several large clinical studies have demonstrated that patients with high-grade carotid stenoses who undergo cardiac surgery have an increased risk of perioperative neurologic injury and death compared with patients without carotid artery disease who have cardiac operations (Table 5). In addition, several studies have shown that patients with bilateral carotid disease, especially those with unilateral stenosis and contralateral occlusion, are at particularly high risk for perioperative neurologic events, regardless of whether the ca-

Table 5. DATA FROM PUBLISHED SERIES REGARDING EARLY NEUROLOGIC EVENT AND STROKE RATES IN PATIENTS UNDERGOING CARDIAC SURGICAL PROCEDURES

	Patients Undergoing Cardiac Surgery								
	General Population or Patients Screened and Negative for Carotid Disease			Patients with Carotid Disease					
				No CEA			CEA		
	n	Mortality Rate	Stroke Rate	n	Mortality Rate	Neurologic Event Rate	n	Mortality Rate	Neurologic Event Rate
Barnes et al., 1985	364	0.2%	1%	85	11%	5%	0	0	0
Brener et al., 1987[2]	3894	4%	2%	96	15%	9%	57	11%	9%
Hertzer et al., 1989[3]	4000	1%	2%	81	4%	7%	170	5%	5%
Faggioli et al., 1990[4]	432	2%	2%	88	5%	7%	19	0	0
Berens et al., 1992[6]	901	5%	2%	140	7%	4%	46	11%	7%
Totals	9591	2.7%	1.9%	490	8.0%	6.1%	292	6.8%	5.8%

n = number of patients; CEA = carotid endarterectomy.

rotid artery disease was treated surgically at the time of the cardiac procedure.[2,5,7]

Carotid duplex scanning has proven to be an accurate, noninvasive method for detecting carotid artery disease.[13] The accuracy, ease of use, and relative low cost of this technique, coupled with the increased incidence of carotid disease in an increasingly older population of cardiac surgical patients, has made duplex scanning a valuable screening test before cardiac surgery.[4,6] Bilateral carotid artery disease was identified in 32 of the 50 patients in our study only because they underwent routine preoperative duplex scanning.

The lack of precise information concerning the mechanisms of neurologic injury in patients with carotid artery disease who undergo cardiac surgical procedures limits the ability to predict accurately the risk perioperative stroke. Both watershed (low flow) and embolic or thrombotic strokes may occur. A high correlation between watershed infarction and hemodynamically significant carotid stenoses might be anticipated because, theoretically, flow should be diminished downstream from the stenosis. A critical reduction in cerebral flow may occur during cardiopulmonary bypass because of reduced arterial pressure and nonpulsatile flow. However, Johnsson et al.[14] and Powers et al.[15] have shown that anatomically defined carotid stenoses do not always compromise cerebral blood flow. Collateral circulatory pathways and cerebral autoregulation can reduce the impact of carotid stenosis on cerebral hemodynamics. Predicting the occurrence of embolic strokes or acute carotid occlusion, which may depend not only on the degree of stenosis, but also on the geometry and surface morphology of the plaque as determined by duplex scanning or angiography, is imprecise. Notwithstanding these imprecisions, results from clinical studies show that patients with high-grade carotid stenosis who undergo cardiac surgical procedures are at increased risk for perioperative neurologic injury and death.

Whether, and under what circumstances, performance of conventional carotid endarterectomy in combination with a cardiac surgical procedure reduces the risk of perioperative stroke is uncertain. Based on our experience and that reported by others,[12,16] we have been impressed with the increased risk and devastating nature of stroke in patients after cardiac surgical procedures. Before instituting the current protocol, three of our patients with unilateral high-grade carotid stenoses underwent a cardiac surgical procedure without carotid endarterectomy and developed major strokes in the cerebral hemisphere ipsilateral to the carotid stenosis. These patients awakened from anesthesia without a stroke, but developed major neurologic deficits in the early postoperative period.[12] Follow-up carotid duplex scans documented occlusion of the previously stenotic carotid artery. The results of the published clinical studies and our experience prompted us to consider other strategies for the management of patients with significant carotid artery disease who underwent cardiac surgery. In patients considered to be at highest risk for perioperative stroke, those with bilateral carotid disease, we evaluated a strategy that employed profound systemic hypothermia and circulatory arrest.

The rationale for the use of profound hypothermia during these combined procedures is based on previous clinical experience and on physiologic studies. Clinically, profound hypothermia has been used in conjunc-

tion with operations on the heart and thoracic aorta to provide protection from ischemia. Studies during cardiopulmonary bypass in monkeys have shown that hypothermia (<20 C) reduces cerebral oxygen consumption by more than 80%.[17] In man, Johnsson et al.[14] have shown that even in the presence of significant bilateral carotid disease, cerebral blood flow measured by the xenon washout technique was preserved during hypothermic cardiopulmonary bypass at 30 C. Together, these studies indicate that the cerebral supply:demand O_2 ratio is improved during hypothermic cardiopulmonary bypass. Similar improvement in this ratio also would be expected for the heart and other organs. The protective effects of hypothermia during carotid clamping can be especially important in patients with bilateral carotid disease who also may have occlusive disease in the vertebral and intracranial arteries. Furthermore, use of hypothermia eliminates the need for an intraluminal shunt and the risks that are associated with its use.

The use of lesser degrees of systemic hypothermia (20 C–28 C) to protect the brain and other organs during combined cardiac and carotid surgery has been reported by others.[18–21] Our protocol employed a period of circulatory arrest in addition to profound systemic hypothermia (15 C–18 C). Circulatory arrest was used during the period of carotid artery clamping to reduce the duration of cardiopulmonary bypass and thus, to decrease exposure to pump-related sources of brain injury during these prolonged procedures.[22,23] Furthermore, at these temperatures, a 30- to 45-minute period of circulatory arrest is safe, whereas the possible detrimental effects of altered cerebral perfusion during carotid clamping (pressure gradients, oxygen-free radical generation), particularly when the other internal carotid artery is totally occluded, are not known. With this technique, there were no perioperative strokes or reversible neurologic deficits. The patients awakened from surgery early, two thirds of them were extubated postoperatively within the first 24 hours, and the median length of stay in the intensive care unit was 3 days. Complications associated traditionally with circulatory arrest, including excessive bleeding, prolonged mechanical ventilation, and temporary global cerebral dysfunction, were infrequent. Despite the increased cardiac-related mortality that has been reported for patients with coronary and carotid artery disease[1,3,4,6,8] and the presence of severe coronary artery disease in the patients in our study (64% had unstable angina and 42% had significant left main coronary artery disease), there was only one cardiac-related death. There have been seven late deaths, none of which was associated with stroke, and two late neurologic events, both of which involved the hemisphere contralateral to the operated carotid artery.

We favor a combined procedure for patients with bilateral carotid disease who require a cardiac operation because we believe that these patients are at substantial risk for stroke in the early postoperative period when bleeding, low cardiac output, extracellular fluid shifts, and arrhythmias can lead to episodes of hypotension, which may precipitate thrombosis of a stenotic carotid artery or result in reduction in flow to areas of the brain supplied by stenotic arteries. Our results suggest that hypothermia may be beneficial in reducing the incidence of cerebral infarction as a result of low flow, as originally envisioned, and also in decreasing the frequency of thromboembolic strokes. The inhibitory effects of hypothermia on platelet function and on the coagulation cascade may offer protection from early thrombus formation at the fresh endarterectomy site in the early postoperative period. By whatever mechanism, the technique of profound hypothermia and circulatory arrest provides adequate protection of the brain and heart during combined carotid and cardiac operations and appears to reduce the frequency of stroke in the high-risk subgroup with bilateral carotid artery disease.

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Discussion

DR. ALLEN S. HUDSPETH (Winston-Salem, North Carolina): I strongly endorse the principle of combined carotid and cardiac surgery performed by a single team. This opinion has evolved from an earlier staged approach wherein carotid endarterectomy was done first, if most urgent, or cardiac surgery was done first, if it was most urgent. However, certain patients were encountered whose disease was such that combined surgery was clearly the safest treatment. I've used a different technique than described by the authors and believe it is preferable to this. Although Dr. Kouchoukos and his group have reported good results using hypothermic circulatory arrest, I believe this is making the simple complex. Profound hypothermic circulatory arrest is a useful tool in cardiovascular surgery, and I use it often for surgery of complex congenital or acquire diseases. However, it is not as safe as hypothermic cardiopulmonary bypass and is not necessary for successful execution of combined carotid and cardiac surgery. Using cardiopulmonary bypass with a core temperature of 25 C, I have performed combined carotid and cardiac surgery on 41 patients whose disease was comparable to those described here. There has been no 30-day mortality, no strokes, or evident neurologic changes. This method gives excellent cerebral protection for careful performance of carotid endarterectomies and allows smooth flow of combined operation. It has proven so simple and safe that I no longer stage the stable patients, but proceed immediately with the combined operation. I would encourage this approach over circulatory arrest.

DR. TIMOTHY J. GARDNER (Philadelphia, Pennsylvania): As many of us know, some of Dr. Kouchoukos's most significant contributions to the field of cardiothoracic surgery has been his innovative work toward the avoidance of neurological injury in patients undergoing cardiac surgery procedures. This series of patients presented today, namely, those with significant bilateral carotid artery occlusive disease who require urgent coronary bypass grafting are a particularly troublesome subgroup of patients at high risk of neurological injury, as was well pointed out by Dr. Kouchoukos. Historically, most of these patients judged to require concurrent carotid endarterectomy and bypass grafting have had the carotid surgery done prior to initiating bypass. Recently, some surgical groups—and Dr. Hudspeth's excellent series is an important contribution—the concept of doing the carotid endarterectomy while on bypass with the patient cooled to a moderate level of hypothermia. I think that this is an important point to emphasize. As far as I know, Dr. Kouchoukos is the first one to advocate profound cooling and circulatory arrest for the performance of the endarterectomy. I think it's remarkable that he's accumulated such a large experience in 50 patients, but even more impressive are the outstanding results he's achieved in these high risk patients. I think the absence of neurological complications in this series of patients mandates that we give it careful consideration as an approach to concurrent endarterectomy and bypass grafting. I think, however, the major unresolved question in my mind which really is not answered by this superb series is whether carotid endarterectomy is unequivocally indicated in all of these patients. Two thirds of these patients with bilateral carotid artery disease were in fact asymptomatic. Many of us would argue that concurrent carotid endarterectomy might not be appropriate in all such instances. Clearly, these asymptomatic patients have managed to compensate with respect to cerebral blood flow despite the significant occlusive, even with unilateral carotid artery occlusion. Furthermore, it is possible to alter intraoperative, and even early postoperative, management in such patients to reduce the risk of bypass-induced reductions in cerebral blood flow or postoperative thrombotic complications. While it is certainly difficult to argue with the superb results obtained in these initial 50 patients, it's doubtful that the use of profound hypothermia and circulatory arrest will prove to be without problems in a larger series of patients managed in this fashion. I think it is notable that at least one or more of these patients in Dr. Kouchoukos's series required circulatory arrest for nearly an hour. I think it is, therefore, very important to make sure that the indications for undertaking such a major and risky operative procedure are appropriate. The other thing I think is worth commenting on is that Dr. Kouchoukos's indication is for routine duplex scanning of the carotid arteries in these elderly patients, that is, patients over 65, or in patients who have the presence of neurological signs