Reduced Strokes in the Elderly: The Benefits of Untouched Aorta Off-Pump Coronary Surgery

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Background. **Avoiding aortic manipulation during off-pump coronary artery bypass (OPCAB) reduces the risk for atheroembolic complications and may, thus, benefit elderly patients who are prone to atherosclerotic aortic involvement.**

Methods. **During a period of 18 months (2000–2002), 160 consecutive OPCAB patients older than 75 years were evaluated. One hundred and three patients undergoing clampless OPCAB were compared to 57 patients in whom side clamps were applied. Clampless revascularization was achieved by in situ or T-graft arterial configurations.**

Results. **Mean age was older (79.3 years vs 78.2, $p = 0.049$) and the prevalence (43% vs 7%, $p < 0.0001$) and severity of aortic disease was higher in the clampless group. The main conduits used were bilateral skeletonized internal thoracic artery (47%) and radial arteries (42%). More grafts were performed in the side-clamp group (2.5 ± 0.5 vs 2.3 ± 0.6, $p = 0.023$), however, revascularization of the postero-lateral territory was comparable. While early mortality (2.9% vs 7%, $p = \geq 0.05$), perioperative myocardial infarction (3% vs 5%, $p = \geq 0.05$), and sternal infections (none) were similar, the incidence of major neurological complications (0% vs 5.3%, $p = 0.044$) and the combined outcome of stroke or mortality (3% vs 12%, $p = 0.035$) were lower in the clampless group. Multivariate analysis identified side clamping as a predictor for the occurrence of stroke or mortality (OR, 6.28, CL 1.39–28.4, p = 0.017), increasing this risk by sixfold.**

Conclusions. **Clampless OPCAB is associated with reproducible neurological benefit. Improved neurological outcome may be conferred irrespective of the method of aortic screening in patients 75 years or older. The use of arterial conduits for this purpose is feasible despite the patients' advanced years.**

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Changing demographics have led to a higher proportion of older and sicker patients referred to coronary artery bypass grafting (CABG) [1]. Subgroup analysis has documented a ninefold increase in the incidence of major neurological complications in patients 75 years or older compared to younger patients following on-pump CABG [2, 3]. Embolic dislodgement of atherosclerotic plaques during surgical aortic manipulations has been recognized as a major source of stroke [3, 4]. Considering the high propensity of moderate-to-severe atherosclerotic aortic disease in the elderly [5], these patients are particularly prone to stroke-related embolization following aortic manipulations [5].

Off-pump coronary artery bypass (OPCAB) obviates the need for aortic cannulation and cross clamping and offsets untoward effects, such as inflammatory responses [6] and aerial or platelet aggregate emboli, related to the cardiopulmonary bypass. Nevertheless, the use of partial aortic clamps is still necessary to construct proximal aortic anastomoses. Albeit few exceptions [7], to date, only modest neurological benefit has been observed following OPCAB in comparison to conventional CABG; consistent and reproducible benefits in terms of major neurologic outcome was not evident [8, 9]. These results have been further corroborated in recent prospective randomized comparative studies [10–12].

While the use of in situ or composite arterial grafts have obviated the need to attach grafts to the aorta [13], thus allowing clampless (untouched aorta) OPCAB, arterial conduits have been traditionally reserved for young patients. We have not denied the use of arterial grafts in elderly patients since 1996 [14] and our department has continued to endorse this strategy during OPCAB since 2000.

The purpose of this study was to compare major neurologic outcome between the clampless and side-clamp OPCAB techniques in patients 75 years or older.

Patients and Methods

Study Design

The data of 467 consecutive patients, who underwent isolated primary OPCAB with multiple grafts between September 2000 and July 2002, were acquired. Within this cohort, 160 patients (34%) were 75 years or older. Of these, 103 patients were operated without aortic manipulation (clampless group) and 57 patients had OPCAB

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using partial aortic clamps during the construction of proximal aortic anastomoses (side-clamp group). Off-pump procedures comprised 51% of the isolated CABG operations performed during this period and arterial revascularization was applied in 76% of the patients.

Proximal mechanical connectors were not used: the term "clampless OPCAB," therefore, denotes an untouched aorta. Patients undergoing single grafts were excluded in order to avoid preselection to the clampless group (all cases were anterior wall revascularizations grafted by in situ left internal thoracic artery). The inclusion of these patients may have biased the results considering that altered hemodynamics during off-pump cardiac displacement constitute a risk factor for stroke. Epiaortic ultrasound was not done routinely. A 7.5-MHz probe (Hewitt-Packard Inc, USA) was used when undetermined findings were encountered during digital aortic palpation or when a high index of suspicion arose following chest radiography or coronary angiography. Thirty percent of the patients were ultrasonographically screened and the findings were interpreted by the surgeon himself. The degree of aortic disease was graded in accordance with the criteria of Mills and Everson [15]. When graded as none or mild (areas free of aortic disease easily identified), the patient was considered suitable for both techniques and patient allocation was based on technical considerations [13]. Clampless OPCAB was performed when the extent of aortic disease was graded as moderate (ie, disease moderately extensive but with adequate disease-free areas) or severe (ie, circumferential disease with no disease-free areas). Thus, by definition, the prevalence and severity of aortic disease was higher in the clampless group. All patients were routinely screened by carotid Doppler assessments. The patients who required carotid endarterectomy, ie, symptomatic with unilateral stenosis greater than 70% or symptomatic with severe bilateral stenosis, were excluded from this study.

Definition of Terms

Patients' data were collected and analyzed according to the STS National Cardiac Surgery database guidelines and definitions (http://www.ctsnet.org/doc/4314). Operative mortality was defined as death occurring within 30 days of the operation. Neurological complications were defined as global or focal neurologic deficit that was evident after emergence from anesthesia and categorized as either permanent or reversible (transient ischemic attacks and prolonged reversible ischemic neurologic deficit). All neurological events were evaluated by a neurologist and further confirmed by computed tomographic scan. Incomplete revascularization was defined as the failure to graft one coronary artery of less than 1 mm in diameter, which was preoperatively planned for grafting.

Surgical Technique and Postoperative Management

Operations were performed through midline sternotomy. Anticoagulation was achieved using 2 mg/kg of heparin and the activated clotting time was maintained above 300 seconds. The heart was stabilized using a suction tissue stabilization system (Octopus, Medtronic Inc, Minneapolis, MN). A deep pericardial retraction suture was placed at the posterior fibrous pericardium medial to the proximal part of the inferior vena cava to help manipulate and rotate the heart to vertical and lateral positions. Right-sided pericardial incision directed towards the inferior vena was selectively performed to facilitate venous return. Vessel occlusion was achieved by external encircling silicone rubber bands. Intracoronary shunts were not used routinely (only in selective cases of right coronary grafting).

The conduits used in the clampless group were the internal thoracic artery (ITA), the radial artery (RA), and (or) the right gastroepiploic artery (RGEA). Grafting arrangements included in situ left-sided bilateral ITA (cross technique) or T-graft configurations constructed of bilateral ITA or left ITA–RA. The RGEA was only used in situ. ITAs were routinely skeletonized [13] and dissection of the RA and the RGEA was facilitated by ultrasonic scalpel (Harmonic Scalpel, Ethicon Endosurgery, Cincinnati, OH). The choice of configuration was determined by technical considerations, previously detailed elswhere [13]. T-anastomoses were constructed (when T-grafts were used) prior to the distal coronary anastomoses. The RA was not attached in any case to the aorta.

Revascularization in the side-clamp group was achieved by ITAs and saphenous vein grafts (SVG). All SVGs were attached to the aorta and constructed proximally following the placement of a side-biting clamp. The left anterior descending (LAD) anastomosis was performed first in the sequence of grafting in both groups.

Three cases of conversion to CABG were documented in the total group (two conversions were elective prior to the initiation of grafting and one was required on emergent basis). These patients were excluded from the study (none died or sustained neurologic injury).

Postoperatively, all patients received intravenously administered isosorbide dinitrate (4 to 20 mg/h) for two days. Oral calcium blockers (Dilatam, Teva, Petah-Tikva, Israel) were given to patients who received RA or RGEA conduits and continued for 6 months. Antiplatelet therapy included Aspirin, 250 mg per day (recommended for indefinite use), and Clopidogrel 75 mg per day (Plavix, Sanofi winthrop, France), for 6 weeks postoperatively.

Follow-up was obtained by a telephone questionnaire.

Data Analysis

Data are expressed as mean ± standard deviation. The χ^2 test and Fisher exact test were used to compare discrete variables. Actuarial survival was obtained with the Kaplan–Meier method. Statistical significance was calculated with the log-rank test. Stepwise logistic regression was used to evaluate the effect of preoperative and intraoperative descriptors on occurrence of neurological complications, early mortality, and the combined endpoint of neurological complications and early mortality. Results of logistic regression were expressed as odds ratio with associated 95% confidence interval limits and p

Table 1. Preoperative Characteristics

Variable	Clampless Group n = 103	Side-Clamp Group n = 57	*p* Value
Age (years) mean	79.3 ± 3.6	78.2 ± 3.6	0.049
range	75–92	75–93	
Age ≥ 80 years	39 (37.9)	17 (29.8)	0.307
Female gender	38 (36.9)	25 (43.9)	0.388
Hypertension	67 (65.0)	37 (64.9)	0.986
Diabetes	28 (27.2)	15 (26.3)	1.000
Peripheral vascular disease	25 (24.3)	7 (12.3)	0.069
Creatinine > 2 mg/dL	8 (7.8)	6 (10.5)	0.554
Chronic lung disease	10 (9.7)	6 (10.5)	0.869
Acute MI (<1 week)	9 (8.7)	5 (8.8)	0.994
Congestive heart failure	23 (22.3)	17 (29.8)	0.294
Left main stenosis (>50%)	32 (31.1)	16 (28.1)	0.692
3-vessel disease	98 (95.1)	54 (94.7)	1.000
Ejection fracton ≤ 35%	12 (11.7)	3 (5.3)	0.260
Emergency operation	8 (7.8)	7 (12.3)	0.348
Preoperative IABP	8 (7.8)	5 (8.8)	0.824
Prior cerebrovascular disease	9 (8.7)	6 (10.5)	0.710
Carotid disease			
Mild (<50% stenosis)	88 (85.4)	51 (89.5)	
Moderate (50%–70% stenosis)	12 (11.7)	5 (8.8)	
Severe (>70% stenosis)	3 (2.9)	1 (1.8)	0.849

Variables are expressed as n (%).

IABP = intra-aortic balloon pump; MI = myocardial infarction.

values. All analyses were performed by SPSS 9 software (SPSS Inc, Chicago, IL).

Results

Preoperative parameters were assessed for their effect on survival and complications by using univariate analysis (Table 1). Baseline characteristics were comparable with the exception of older age (79.3 vs 78.1 years, $p = 0.049$) and a higher prevalence of peripheral vascular disease (statistical trend) in the clampless group (Table 1).

Operative data are listed in Tables 2 and 3. The prevalence and severity of aortic disease were higher in the clampless group. Moderate-to-severe atheromatous involvement was detected in 36% of these patients, while graded as free of or mild in all but one patient in the side-clamp group (Table 2). Despite a higher mean number of grafts in the side-clamp group (2.54 ± 0.5 vs 2.3 ± 0.6, $p = 0.003$), revascularization of the postero-lateral territory (ie, grafting obtuse marginal or posterior descending arteries) (Table 2) and the completeness of revascularization (Table 2) were comparable. Arterial conduits were inherently used more often in the clampless group (Table 2). The type of conduit, grafts' configuration, and the corresponding target coronary arteries are described in Tables 2 and 3.

Operative Mortality and Morbidity

Data on operative mortality and morbidity are listed in Table 4. Early mortality was lower in the clampless group

Table 2. Operative Data

Variable	Clampless Group n = 103	Side-Clamp Group n = 57	*p* Value
Epiaortic ultrasound	33 (32)	14 (24.6)	0.320
Grafts/patient ratio			
Mean	2.30 ± 0.6	2.54 ± 0.5	0.003
Range	2–4	2–3	
Atherosclerotic aorta	45 (43.6)	4 (7)	<0.0001
Aortic grading			
Moderate atherosclerosis	21 (20.3)	1 (1.7)	0.0013
Severe atherosclerosis	16 (15.5)	0	0.0014
Use of left ITA	103 (100)	57 (100)	
Use of right ITA	48 (46.6)	15 (26.3)	0.012
Use of bilateral ITA	48 (46.6)	15 (26.3)	0.012
Use of radial artery	43 (41.7)	—	<0.0001
Use of RGEA	5 (4.9)	—	0.161
Use of SV	1 (0.9)	57 (100)	<0.0001
T-grafts	65 (63.1)	6 (10.5)	<0.0001
Sequential grafting	40 (38.8)	4 (7.0)	<0.0001
BITA cross configuration	27 (26.2)	10 (17.5)	0.212
Pts receiving grafts to postero-lateral territory	89 (86.4)	49 (86)	0.938
Incomplete revascularization	5 (4.8)	2 (3.7)	1.000
Target coronary vessel			
LAD	102 (99)	57 (100)	1.000
Diagonal	21 (20.4)	4 (7)	0.038
Circumflex	88 (85.4)	42 (73.7)	0.068
RCA	4 (3.9)	12 (21)	0.0009
PDA	23 (22.3)	30 (52.6)	0.0001

Variables are expressed as n (%).

ITA = internal thoracic artery; LAD = left anterior descending; PDA = posterior descending artery; RCA = right coronary artery; RGEA = right gastroepiploic artery; SV = saphenous vein.

although the difference did not reach statistical significance. The Euroscore predicted mortality was 9.1% ± 8.1% (CL, 0.075–0.106) in the clampless group, significantly higher than the observed 2.9%, and 8.9% ± 11.5% (CL, 0.085–0.119) in the side-clamp group. The modes of death were multiorgan failure (3 patients), cardiac related (2 patients), and an acute mesenteric event diagnosed during laparotomy (2 patients).

All the neurological complications occurred in the

Table 3. Conduits Used and the Corresponding Target Coronary Vessels

	LITA	RITA	RA	GEA	SVG
LAD	116 (73)	43 (27)	0	0	1 (0.6)
Diagonal	20 (13)	0	5 (3)	0	0
Cx marginal	40 (25)	17 (11)	44 (28)	0	29 (18)
RCA	0	4 (3)	0	0	12 (8)
PDA	0	1 (0.6)	17 (11)	5 (3)	30 (19)

Variables are expressed as n (%).

Cx = circumflex; GEA = gastroepiploic artery; LAD = left anterior descending; LITA = left internal thoracic artery; PDA = posterior descending artery; RA = radial artery; RCA = right coronary artery; RITA = right internal thoracic artery.

Table 4. Early Results

Variable	Clampless Group n = 103	Side-Clamp Group n = 57	Total n = 160	*p* Value
Length of hospital stay (days)				
Mean	5.41 ± 2.12	6.07 ± 3.89	5.65 ± 2.89	0.241
Range	0–20	0–24		
Early mortality	3 (2.9)	4 (7)	7 (4.4)	0.248
Myocardial infarction	3 (2.9)	3 (5.3)	6 (3.8)	0.667
Atrial fibrillation	18 (17.4)	10 (17.5)	28 (17.5)	0.991
Re-exploration d/t bleeding	1 (1)		1 (0.6)	1.000
Renal failure[a]	7 (7)	4 (7.4)	11 (7.1)	1.000
Sternal infection				
Deep				
Superficial	2 (1.9)	2 (3.5)	4 (2.5)	0.617
Major neurologic event		3 (5.3)	3 (1.9)	0.044
Neurologic event or mortality	3 (2.9)	7 (12.3)	10 (6.3)	0.035

[a] Defined as serum creatinine level of 2 mg% or more or and postoperative increase of 1 mg%.

Variables are expressed as n (%).

side-clamp group with a significantly higher incidence (0/103 vs 3/57) (Table 4). The neurologic deficit was permanent in two patients and reversible, albeit prolonged, in one patient. Two patients who suffered a stroke had been regarded by the surgeon as being free of aortic disease, and in one stroke patient the aorta was considered as being mildly involved.

The incidence of stroke or mortality was significantly higher in the side-clamp group (12.3% vs 2.9%, $p = 0.035$) (Table 4).

Prediction of Stroke and Mortality

Stepwise logistic regression was used to assess the effect of confounding factors on stroke, mortality, and the combined end point of stroke or mortality. These results are shown in Table 5. The use of a side clamp (surgical technique) (odds ratio, OR 6.3), a history of cerebrovascular disease (OR 6.3) and diabetes (OR 5) were identified as independent risk factors for stroke or mortality. Patients with a history of cerebrovascular disease had a higher propensity for stroke (OR 22). Finite OR and confidence interval could not be calculated for other variables, apparently due to the small number of outcome events (Table 5).

Follow-Up Status

Follow-up was 97% complete (2 patients in the clampless group and 3 in the side-clamp group were lost to follow-up) and ranged between 5 to 28 months (mean, 16 ± 7.7 months). The midterm results are presented in Table 6. There were 4 (3.9%) and 6 (10.5%) late deaths in the clampless and side-clamp groups, respectively ($p = 0.169$). The two-year survival (Kaplan-Meier) of the total OPCAB group was 88.7% ± 4.1%. Both groups were

Table 5. Stepwise Logistic Regression: Independent Risk Factors for Stroke, Mortality, and Combined Outcome of Stroke or Mortality

	Stroke			Mortality			Stroke or Mortality		
Variable	OR	95% CL	*p*	OR	95% CL	*p*	OR	95% CL	*p*
Age				0.91	0.68–1.21	0.508	0.89	0.68–1.18	0.443
Sex				1.19	0.10–13.9	0.891	2.89	0.25–33.4	0.395
Diabetes				10.5	0.66–167	0.096	5.05	1.22–20.7	0.025[a]
Hypertension				6.90	0.18–261	0.298	7.59	0.26–218	0.237
PVD						0.879	0.50	0.01–13.2	0.683
Renal failure				1.87	0.06–59	0.723	2.01	0.07–57.7	0.682
Chronic lung disease				20.0	0.38–1057	0.139	10.4	0.18–581	0.252
Cerebrovascular disease	22.1	1.88–261	0.014[a]	3.54	0.09–129	0.491	6.32	1.23–32.5	0.027[a]
Atrial fibrillation				7.98	0.38–169	0.182	16.3	0.53–496	0.019
CHF				0.76	0.03–18.7	0.868	0.94	0.60–14.8	0.969
Left main disease				0.57	0.04–9.26	0.692	0.87	0.063–12.3	0.924
Emergent operation				6.57	0.17–259	0.315	26.5	0.39–1787	0.127
Operative variables									
Use of BITA				0.92	0.05–15.8	0.953	2.31	0.16–31.8	0.531
T-grafting				0.41	0.01–15.9	0.632	2.00	0.10–39.5	0.649
Grafting of posterolateral territory				1.64	0.11–24.8	0.721	0.64	0.04–9.34	0.745
Epiaortic ultrasound				2.02	0.13–30.6	0.611	9.26	0.47–182	0.143
Use of side-clamp				1.13	0.06–20.1	0.934	6.28	1.39–28.4	0.017[a]

[a] Significant value ($p < 0.05$).

BITA = bilateral internal thoracic artery; CHF = congestive heart failure; CL = confidence limit; OR = odds ratio; PVD = peripheral vascular disease.

Table 6. Mid-Term Results

Variable	Clampless Group n = 103	Side-Clamp Group n = 57	*p* Value
Recurrent angina	4 (3.9)	5 (8.8)	0.283
Myocardial infarction	2 (1.9)	2 (3.5)	0.167
Repeat angioplasty			
Repeat operation			
Neurologic events			
Late mortality[a]	4 (3.9)	6 (10.5)	0.169
Cardiac-related death	1 (2.9)	5 (8.8)	0.134
Noncardiac death	1 (1)	1 (1.8)	1.000

[a] Defined as death occurring more than 1 month after surgery.

Variables are expressed as n (%).

comparable with regard to all causes of mortality, cardiac-related mortality, major cardiac events, and the occurrence of late stroke (Table 6).

Comment

The findings of this study suggest that clampless OPCAB is associated with a reduced risk for major neurological complications in patients 75 years of age or older. The use of partial aortic clamps in this subgroup increases the propensity for stroke or mortality.

The impact of partial aortic clamping on the incidence of major neurological complications has been observed before. Calafiore and associates have shown that the subsequent risk is comparable to that following the entire cannulation and cross clamping required for cardiopulmonary bypass [16]. In situ and T-graft arterial configurations were originally proposed to improve graft patency and have, therefore, been traditionally reserved for young patients. While arterial conduits are essential to achieve "no-touch" aorta revascularization considering that composite attachment of venous grafts is currently unacceptable, the use of these conduits in elderly subsets of patients has been a matter of debate. The clampless group described herein is unique in view of the fact that total arterial revascularization was performed in old patients (mean age, 79 years), on routine bases, by all surgeons and over a short period of time.

There were no major neurological complications among 103 patients in the clampless group, irrespective of the severity of atherosclerotic aortic involvement or the method used for aortic screening. These results were achieved despite the fact that the clampless group constituted a higher risk for stroke by being older in age [3] and by having a higher prevalence of aortic disease [3] and peripheral vascular disease [17], while other recognized predictors of stroke, ie, history of cerebrovascular disease [18], diabetes [17], hypertension [19], atrial fibrillation, and carotid disease were evenly distributed between the groups. Consistent with previous observations [18], a history of cerebrovascular disease was identified as a correlate of stroke (multivariate analysis). The small number of outcome events may have obscured other contributing factors. The surgical technique (the use of side clamp), however, was identified as an independent predictor for stroke or mortality, increasing this risk by sixfold.

The incidence of stroke reported herein should be viewed in face of 9% [2] and 8% [3] age-adjusted rates reported in corresponding groups undergoing conventional CABG. Data on the incidence of stroke in elderly patients undergoing OPCAB are conflicting. A wide variation in this incidence has been documented, ranging from no strokes [20, 21] to a recent report of 4% [22]. As a result, conclusions regarding the neurological benefit of OPCAB in comparison to conventional CABG have been contradictory [20–22]. Partial aortic clamps, however, were frequently applied in these studies [20–22]. Considering as well our 5.3% stroke incidence in the side-clamp group, the reasons for these variations may be attributed to different aortic screening strategies (nonspecified in the above-mentioned reports). Epiaortic ultrasound has been established as the modality of choice for this purpose and has been previously recommended in patients 70 years or older [5]. Nevertheless, decisions are made based on qualitative sonographic information and, in many cases, upon the sole evaluation of the surgeon; therefore, misinterpretation and subsequent errors may occur. Epiaortic ultrasound provides valuable information to warrant modifications in the surgical technique, but not all strokes may be prevented [5]. Interestingly, epiaortic ultrasound is not routinely applied in all centers [23]. The findings of our current study suggest that clampless OPCAB provides reproducible neurologic benefit irrespective of the detection method used.

Fewer grafts were performed in the total arterial (clampless) group, but revascularization of the challanging postero-lateral cardiac territory and completeness of revascularization were still comparable. Furthermore, the grafts per patient ratio appears similar to other OPCAB series of this age group [22]. It is suggested, therefore, that the use of arterial and sequential grafting during OPCAB in elderly patients can be applied at an acceptable level of risk.

Several limitations of this study need to be addressed. It is a retrospective study with a limited number of patients and a small number of outcome events. Larger cohorts would be required to validate these preliminary findings. It is likely that certain cases of atherosclerotic aortic disease went undetected and resulted in stroke. Thus, epiaortic ultrasound prior to aortic manipulation is warranted in these patients. Nevertheless, clampless OPCAB may still be the modification of choice once aortic disease was sonographically detected [24]. Relevant issues for further assessment would be the role of newly available proximal mechanical connectors, which enable clampless construction of proximal aortic anastomoses [25] and the effect of clampless OPCAB on neurocognitive outcome.

In conclusion, clampless OPCAB in elderly patients may attenuate the risk for major neurological complications irrespective of the aortic screening strategy. The use of arterial configurations, which bypass the need for

proximal aortic anastomoses, should be considered in these patients despite their old age.

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