Coronary artery bypass grafting with carotid artery endarterectomy – does combined approach places a patient at greater risk of hemorrhagic complications than an isolated procedure?

Pomostowanie aortalno-wieńcowe wraz z endarterektomią tętnic szyjnych – czy połączone podejście stwarza większe ryzyko powikłań niż procedura izolowana?

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Abstract

Background: The appropriate management of patients with concomitant coronary and carotid vascular disease remains a subject of evaluation. The purpose of presented study was to compare hemostatic status and range of hemorrhagic complications following an isolated coronary revascularization and combined procedure of coronary artery bypass grafting with concomitant carotid artery endarterectomy.
Material and Methods: Records of 60 patients were analyzed retrospectively. Two groups were elected; first – A consisted of patients undergoing CABG and CAE as a concurrent procedure and the second one of those treated with CABG alone – B. Presented study compares various values of hemostasis and blood loss parameters on four different stages of hospitalization.
Results: Patients undergoing concomitant procedure presented with greater hemorrhagic complications mainly in the first postoperative day : total chest tube drainage was higher in Group A (1183 ml ±1223 ml vs. 888 ±529; p = 0.23), as was a total number of Red Blood Cells units used in treatment of postoperative anemia (2.57 ±3.23 vs. 1.77 ±1.33); APTT (39.1 seconds ±7.6 vs. 34.5 seconds ±9.1; p < 0.001); Pt (59 µg/ml ±9 vs. 80 µg/ml ±10; p < 0.001); and Hgb (9.8 g/dl ±0.8 vs. 10.8 g/dl ±1.3; p < 0.001). There was no difference in consumption of red blood cells units among the groups.
Conclusions: We conclude as follows: 1. Hemorrhagic complications following simultaneous revascularization present at the greatest intensity during the first postoperative day. 2. Combined procedure should be regarded as a relatively safe tool in management of patients at risk of life – threatening vascular episode.
Key words: CABG, CAE, hemostasis.

Streszczenie

Wstęp: Podejście do pacjentów z chorobą wieńcową współistniejącą z patologią w tętnicach szyjnych stanowi temat opisanego poniżej badania. Jego celem było porównanie stanu hemostazy i zakresu powikłań krwotocznych po izolowanej rewaskularyzacji serca oraz połączonej procedurze graftowania aortalno-wieńcowego z endarterektomią tętnic szyjnych.
Materiał i metody: Grupa 60 pacjentów została poddana analizie retrospektywnej. Wyodrębniono dwie grupy: A – pierwszą, składającą się z pacjentów poddanych jednoczasowej procedurze CABG i CAE, oraz drugą – B – składającą się z pacjentów poddanych tylko operacji CABG. Stwierdzano różne wartości parametrów hemostazy na czterech różnych etapach hospitalizacji.
Wyniki: U pacjentów poddanych połączonej procedurze stwierdzono większą liczbę powikłań krwotocznych w pierwszym dniu po operacji; całkowity drenaż w grupie A wynosił 1183 ml ±1223 ml *vs* 888 ±529; p = 0,23), tak jak ilość przetoczonych jednostek masy płytkowej używanej do skompensowania spadku morfologii krwi (2,57 ±3,23 *vs* 1,77 ±1,33); APTT (39,1 sek. ±7,6 *vs* 34,5 sek. ±9,1; p < 0,001); Pt (59 µg/ml ±9 *vs* 80 µg/ml ±10; p < 0,001) i Hgb (9,8 g/dl ±0,8 *vs* 10,8 g/dl ±1,3; p < 0,001).
Wnioski: Uważamy że: 1) komplikacje krwotoczne następujące po połączonym zabiegu objawiają się najsilniej w czasie pierwszej doby pooperacyjnej; 2) połączona procedura może być uważana za względnie bezpieczną u pacjentów z wyższym ryzykiem powikłań naczyniowych i chorobą wieńcową.
Słowa kluczowe: CABG, CAE, hemostaza.

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Introduction

Current indications for surgical revascularization of isolated carotid or coronary artery disease are well described. Many randomized clinical trials demonstrated that carotid endarterectomy (CEA) decreases stroke risk in patients with symptomatic [1, 2] and, to a lesser extent, asymptomatic [3] severe carotid stenosis. Indications for coronary artery bypass grafting (CABG) are well defined in the cardiac surgery literature as well [4]. However, the optimal management of patients with concomitant coronary and carotid vascular disease has not yet been established. Importance of this clinical problem is underlined by the fact that patients frequently present with atherosclerosis of both arterial systems: 8% to 14% of CABG patients suffer from significant carotid stenosis [5, 6] and 40% to 50% of CEA patients have coronary artery disease [7, 8]. One of the most important questions regarding simultaneous surgical revascularization – CABG + CAE concerns patients' safety in terms of maintaining various hemostatsis parameters at near physiological level. Clotting abnormalities and post surgical blood loss are one of the crucial points in perioperative care of those admitted to both CABG and CABG plus CAE.

Materials and Methods

Records of 60 patients, obtained between January 2005 and July 2008, were analyzed retrospectively. This was a single – center observational study. Subjects were recruited from heterogeneous population treated in Clinic of Cardiac Surgery, University Hospital, Wroclaw, Poland. All patients received detailed information regarding procedures, potential risks and benefits. The study was approved by the Institutional Review Committee and the Bioethics Committee of the Medical University of Wroclaw.

Tab. I. Measured variables

Laboratory parameters
Potential of hydrogen (pH)
Base Excess (BE)
Prothrombin (Pt)
Activated Partial Thromboplastin Time (APTT)
Platelet count (PLT)
Blood loss parameters
Hemoglobin (Hgb)
Hematocrit (Ht)
Total Chest Tube Drainage

Tab. II. Gender distribution and mean age

	N	Mean age (years)	Males (%)	Females (%)
Group A (CABG + CAE)	30	69.36 ±7.05	51.67	48.33
Group B (CABG)	30	65.23 ±10.15	73.33	26.67

Measured variables

A total of 60 patients were divided into two groups. Group A consisted of patients who underwent Coronary Artery Bypass Grafting [CABG] simultaneously with Carotid Artery Endarterectomy [CAE] (n = 30), while group B comprised of those who underwent Coronary Artery Bypass Grafting as an isolated procedure (n = 30) operated in the same frame of time. All patients underwent surgery as an elective treatment. Typical parameters of hemostasis (Tab. I.) were recorded at four different stages of hospital treatment, which were respectively: admission, first postoperative day, second postoperative day and on discharge. Measured variables were of two different kinds: Prothrombin (Pt), Activated Partial Thromboplastin Time (APTT), Acidobasic equilibrium by means of potential of hydrogen (pH), Base Excess (BE) and Platelet Count (Plt) were used to establish hemostatic status of a patient, while Hemoglobin (Hgb), Hematocrit (Hct) and Chest tube drainage (Ctd) were brought to assess hemorrhagic complications.

Subjects

Gender distribution and mean age are shown in Table II.

Preoperative risk factors were not significantly different in both groups, although in group B higher incidence of diabetes mellitus was observed (Tab. III). Patients suffering from any other pathology, especially other heart diseases and coagulation disorders, were disqualified from the study. The other criteria for exclusion were: low ejection fraction (EF) < 40%, advanced age > 85 years and necessity of anticoagulation therapy. Coronary angiography was performed in every subject. Coronary artery disease (CAD) was assumed significant if the vessel stenosis was equal to or greater than 50% of each affected artery lumen. None of the patients had left main stenosis, and none had undergone cardiac/carotid revascularization before. Amongst CABG + CAE group two patients had single, eleven double, and seventeen triple – vessel disease. In CABG group, distribution of severity of coronary disease was: 3, 9 and 18 patients with single, double and triple – vessel disease respectively. Mean Left Ventricular Ejection Fraction was 60 ±12% in A, and 58 ±16% in B. In every patient withdrawal of antiplatelet drugs, vitamin K inhibitors and any other anticoagulant drugs was performed in a safe interval before the operation.

Severity of extracranial cerebrovascular disease in Group A was assessed by Carotid Artery Duplex scanning. Unilateral Carotid stenosis equal to or greater than 70% of artery lumen were observed in 76,66% (23) of subjects, while 23.33% (7) had bilateral disease. In last group three patients suffered from occlusion of one carotid artery with

Tab. III. Preoperative risk factors

Preoperative Risk Factors	Group A (CABG +CAE)	Group B (CABG)	p value
Myocardial Infarction (one or more)	60.00% (18)	56.66% (17)	ns
Arterial Hypertension	30.00% (9)	30.00% (9)	ns
Diabetes Mellitus	33.33% (10)	43.33% (13)	ns
Cigarette Smoking	60.00% (18)	53.33% (16)	ns
Mean Efflux Fraction	60% ± 12	58% ±16	ns
Single – vessel Disease	6.66% (2)	10.00% (3)	ns
Double – vessel Disease	36.66% (11)	30.00% (9)	ns
Triple – vessel Disease	56.66% (17)	60.00% (18)	ns

contralateral stenosis > 70% (Tab. IV). No lesions of vertebral arteries were reported, rostral direction of blood flow was retained as well.

Tab. IV. Severity of extracranial cerebrovascular disease

Level of carotid artery stenosis	
Unilateral Stenosis ≥ 70%	76.66% (23)
Bilateral Stenosis ≥ 70%	23.33% (7)
Occlusion with contralateral stenosis ≥ 70%	10.00% (3)
Clinically asymptomatic patients	80.00% (24)
History of Transient ischemic attack	10.00% (3)
History of stroke	10.00% (3)

Surgical technique

After endotracheal intubation mechanical ventilation was applied with $Fi0_2$ initially 1.0 and then 0.6 and V_T 6-8 ml kg^{-1}, f 10-12 min^{-1} to maintain normal PaO_3 and $PaCO_3$ values. General anesthesia was maintained using a continuous *i.v.* infusion of propofolum (4-12 mg kg^{-1} h^{-1}), and mixture of fentanylum (2 mg) and pancuronium (8 mg) in 50 ml of 0.9% NaCl. Occasionally sevofluranum was administered in various doses.

Carotid endarterectomy was performed prior to the cardiac surgery. An incision running obliquely from the angle of one's jaw towards breastbone was made. The incision was usually 7-10 cm in length. Carotid artery was displayed. In order to enhance safety of the plaque removal, clamping of the carotid communis and the carotid internal artery was performed and small drain inserted into the lumen of the vessel. Longitudinal opening was incised and the narrowing removed. The endarterectomy was performed with surgeons preference (two surgeons were involved in the procedure alternately). Most frequently simple removing of atheromatosis masses from artery was done, less frequently carotid endarterectomy with eversion of the vessel was performed. To protect the brain from interruption to its blood supply, while the artery is clamped, a shunt was used to maintain blood flow. The shunt lied in a loop outside the artery. After the endothelium was cleared, the incision of the artery's wall was closed with very fine prolene suture, either directly or with a patch to prevent narrowing. The patch, if used, was a dacron sheet. The wound was closed by placing absorbable buried suture. The redon catheter with passive suction was used to collect bleeding form closed wound.

Heparin was administered as follows: an initial bolus of 9,000 units/m^2 of body surface area (BSA) and an oxygenator circuit priming dose of 10,000 units. Extracorporeal circulation was conducted with a Dideco membrane oxygenator Stockert CPB machine. The CPB circuit was primed with 1.5 L of plasmalyte, 10 mEq of sodium bicarbonate ($NaHCO_3$), and 12.5 g of mannitol. Additional heparin (5,000 units) was administered when the activated coagulation time (ACT) was less than 450 seconds. After establishing CPB and cross clamping aorta, the protection was applied with warm blood cardioplegia solution – Calafiore plegia. Distal anastomoses were made to the occluded arteries. After removal of the cross clump and return of the cardiac rhythm, proximal anastomoses were performed on the side biting clamp. After deairing of the bypasses patient was disconnected from CPB. In all cases two drains were placed in the left pleural cavity and mediastinum. The operation was finished in typical fashion. The initial protamine dose was 0.01 mg per unit of heparin administered. Heparin neutralization was designated adequately if the post – protamine ACT value was within 10% of the preheparin ACT value.

After the completion of the surgery patients of both groups were transported to the postoperative cardiosurgical intensive care ward, were the ventilation was maintained with the volume controlled ventilators ($Fi0_2$ 1,0; V_T 6-8 ml kg^{-1}; f 10-14 min^{-1}, PEEP 2.5-5 cm H_20 (0,25-0,5 kPa). The oxygen concentration was reduced according to the level of arterial blood gases. The patients were extubated after regaining

complete consciousness and achieving hemodynamic stability, normal body temperature (36.5°C) and spontaneous breathing with satisfying arterial blood gases parameters PaO_2 > 75 mm Hg (10 kPa) at FiO_2 < 0.45. After extubation intensive respiratory physiotherapy was carried out. To achieve appropriate analgesia intravenous non-narcotic analgesics were administered – paracetamol, and ketoprofen. On the first or second postoperative day patients were transferred to the Cardiologic Critical Care Unit (CCU) and after removal of drains from the chest to the general ward. During this time all patients underwent at least two cycle of rehabilitation – respiratory physiotherapy. The chest drains were removed on the second postoperative day when the drainage volume was minimal.

Clinical questions

Presented study compares two types of procedures: isolated CABG and combined CABG and CAE in terms of postoperative hemostasis and hemorrhagic complications. It was designed in order to determine the genuine safeness of combined procedure in terms of parameters responsible to nonsurgical bleeding.

Statistical analysis

Before any further analysis all data were tested for normal distribution with the Shapiro-Wilk test. Results were displayed as mean, standard deviation and median. Statistical significance were assessed by unpaired Student's *t*-test (for normally distributed data) and by Mann-Whitney's test (the rest). Statistical significance was assumed at $p < 0.05$.

Results

Both groups did not reveal any statistical differences on the day of admission. Surgical procedures differed significantly in duration, p value $2{,}595 \times 10^{-9}$. The average time for concomitant surgery was 263 ±54 minutes, while isolated CABG was performed in mean time of 187 ±44 minutes.

Shortly after surgery, on the first postoperative day, subjects undergoing concomitant procedure presented with statistically significant hemorrhagic complications of greater severity and worse hemostatic status than controls (Tab. V).

On the following, second postoperative day, only Arterial Blood Gases differed significantly (Tab. VI).

On the last day of hospital stay, patients of group A were presenting with higher hematocrit than those of group B (Tab. VII).

However without statistical significance (p = 0.25) total chest tube drainage was higher in Group A (1183 ml ±1223 ml vs. 888 ±529; p = 0.23), as was a total number of Red Blood Cells units used in treatment of postoperative anemia (2.57 ±3.23 vs. 1.77 ±1.33), yet still without statistical significance (p = 0.29).

Tab. V. First postoperative day

	CABG + CAE			CABG			p
	AVG	SD	Median	AVG	SD	Median	
BE (mEq/l)	–3.99	±1.973	–4.27	–0.05	±2.418	0.25	10^{-7}
APTT (sec)	39.11	±7.625	37.3	34.55	±9.058	32.3	3.84×10^{-3}
Pt (µg/ml)	59.07	±8.886	59.5	80.04	±10.398	80	6×10^{-11}
Hgb (g/dl)	9.77	±0.847	9.87	10.84	±1.264	10.9	3.3×10^{-4}
HCT (%)	29.28	±2.850	29.9	31.31	±4.139	32.3	3.15×10^{-2}

Tab.VI. Second postoperative day

	CABG + CAE			CABG			p
	AVG	SD	Median	AVG	SD	Median	
pH	7.39	±0.056	7.38	7.44	±0.0925	7.44	2.78×10^{-2}
BE (mEq/l)	–2.33	±2.337	–2.45	–0.25	±2.9728	–0.2	5.39×10^{-3}

Tab.VII. Day of discharge

	CABG + CAE			CABG			p
	AVG	SD	Median	AVG	SD	Median	
HCT (%)	33.37	±3.768	32.4	31.3	±3.119	30.9	2.5×10^{-2}

Discussion

In his review Moore et al. [9] showed significantly greater stroke rate after staged revascularization performed by means of carotid endarterectomy preceded by coronary artery bypass. If staged procedure is executed in different order not only myocardial infarction frequency is greater but also is the death rate [9]. As we read in report of Guibaud [10] and colleagues simultaneous operation with extracorporeal circulation used for additional cerebral protection may be considered as another step towards overcoming neurological adverse effects and effective lowering of perisurgical mortality.

Three studies show that combined CEA and CABG operation can be done with acceptable stroke and mortality rates [11-13]. Akins and associates [11] report a perioperative stroke rate of 3% and mortality rate of 3.5% with concomitant CEA and CABG. There was no randomization of the 200 patients, and 58% of the patients had asymptomatic carotid artery stenosis, a group that would be expected to have a low stroke rate with CABG alone [14]. A similar study by Trachiotis and coworkers [12] shows a 4.5% stroke rate and a mortality rate of 3.4% accompanying combined operation. This was not a randomized trial, and the indications for the combined procedures were not clear in these 88 subjects who were suffering from symptomatic and asymptomatic carotid artery stenosis. Daily and coworkers [13] also report acceptable mortality and stroke rates with combined CEA and CABG as well as reduced hospital costs using this approach. Most of previous studies comparing OPCAB surgery to CABG surgery were retrospective.

Issue regarding safety of such operation in terms of postoperative hemostasis and bleeding is relatively less elucidated. All operations in both groups were performed with the aid of ECC. Extracorporeal circulation and heparin may induce many abnormalities in the coagulation system, including thrombocytopenia, platelet dysfunction [15, 16], coagulation factor deficiencies, residual heparin/rebound after protamine administration [17] and fibrinolysis [18]. Insufficient surgical hemostasis also causes bleeding after CPB. Impaired platelet function is thought to be the most common coagulation defect associated with CPB [19]. Other causes of nonsurgical bleeding are primary fibrinolysis, thrombocytopenia, residual heparin/rebound and more seldom disseminated intravascular coagulation.

Several factors should be taken under consideration which alter such operation from regular CABG procedure. The administration of heparin is done earlier than opening of the chest, harvesting of the internal thoracic artery, harvesting of the veins are performed in more pro – bleeding environment. Surgery duration is another factor which can lead to abnormalities in hemostasis. That applies to the combined surgery which is prolonged as a result of the additional vascular part. In presented study the groups were alike. Gender distribution and mean age were similar in both groups. Most of the patients admitted to our department had triple vessel disease. Also regarding to their neurological history we assumed that the study covered mainly asymptomatic patients. The main focus of our interest, safety of combined surgical procedure, was approach by means of detectable disorders of hemostasis. According to preoperative expectations, differences regarding hematologic status were noted in postoperative period. Predominant differences were seen in the first postoperative day. The following variables were higher among patients submitted to concomitant procedure: the prothrombin (59.07 vs. 80.04) was higher in group B. In group A APTT was higher than in subjects form group B (39.11 vs. 34.55). Hematocrit and level of hemoglobin was lower in group A *vs*. group B. Gradual amelioration of these measured variables were observed on the second postoperative day, when only arterial blood gases differed significantly. Interestingly the hematocrit assessed on the last day of hospital stay was higher in group A (33.4 ±3.8) vs. group B (31.3 ±3.1) – p value < 0.05 which might be due to more severe preceding anemia.

Tab. VIII. Neurological outcome

	CABG + CAE	
	AVG (%)	No. of patients
TIA	6.66	2
Stroke	10.00	3

This shows that longer operation is not related to lower hematocrit value and is not directly related to the amount of blood which was drained from the wound after the completion of surgery. There was no difference in the usage of red blood cells units among the groups (2.6 ±3.2 in group A vs. 1.7 ±1.3 in group B; p = 0.24). In group A the blood loss were higher *vs*. group B (which was 1183 vs. 888) this particular outcome did not reach statistical significance with p value = 0.23.

Several limitation of this study should be mentioned. This was not a randomized trial. Hypothetically best comparison in such case would be to compare patients admitted to CABG and CAE as concomitant surgery to the group of patients were both operations were performed as staged procedure. Having in mind well being of our patients we did not decide to submit any of them to therapy burden with worse outcome as explained earlier.

Hemostasis abnormalities in patient submitted to concomitant CABG and CAE in comparison with CABG alone are predominantly observed in the first postoperative day. During the course amelioration of the clotting parameters is observed. Worse hemostatic condition did not alter the clinical status of the patients presented in this investigation. No major disturbances of the patients condition were seen until the discharge on the sixth postoperative day.

The decision of performing combined procedure should depend on standard risk factors, which include age, urgency and severity of the coronary artery disease, the left ventricular function, and the presence of comorbid medical disorders, especially those which may increase possibility of

excessive bleeding. In conclusion we demonstrated that the combined procedure even though burdened with longer duration and more excessive exposure to heparin, should be treated as relatively safe procedure. The postoperative alterations of hemostasis parameters should also be taken into consideration, as a one of many risk factors upon which we decide whether to proceed or not with combined operations.

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