Early outcomes of isolated coronary artery bypass grafting in Chinese aged patients with diabetes mellitus

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ABSTRACT

الأهداف: مقارنة المؤشرات الأولية لتركيب مجازة الشريان التاجي (CABG) في مرضى السكر الكبار وتقدير أثر السكر على المؤشرات الأولية لـ (CABG) لدى المرضى الكبار.

الطريقة: تم إجراء الدراسة قسم جراحة الأوعية الدموية – مستشفى فيرست بيبول المرتبط – جامعة شنقهاي جايو تونج – شنقهاي – الصين خلال الفترة من يناير 2000 إلى يوليو 2008. تم تقسيم بيانات 593 مريض تبلغ أعمارهم فوق 70 عام خضعوا لتركيب مجازة الشريان التاجي إلى مجموعة مرضى السكر والمجموعة الغير مصابة بمرض السكر. تم تحليل المتغيرات قبل وخلال وبعد العملية لكلا المجموعتين. تم استخدام اختبار (t) و (x^2) و تحليل الانحدار الوجستي المكافئ لتحديد الاختلافات بين المجموعتين.

النتائج: لا يوجد أي اختلاف إحصائي لما قبل العملية وخلالها بين المجموعتين فيما أنه وجدت أمراض الشريان التاجي قي المجموعة المصابة بالسكر. كما لا يوجد أي اختلافات بين المجموعتين للقيم ما قبل العملية مثل المرضية و المضاعفات و نقل الدم. إن نقل الدم والتقدم في العمر ليس عوامل خطر في الوفيات.

خاتمة: أن تركيب مجازة الشريان التاجي للمرضى الكبار السن أمر مشروع. إضافة إلى ذلك، حصل للمرضى المصابين بالسكر النتائج الجراحية نفسها للمرضى الغير مصابين بالسكر.

Objectives: To compare the early outcomes of coronary artery bypass grafting (CABG) in aged diabetic patients, and evaluate the affection of diabetes on the early outcomes of CABG in aged patients.

Methods: The study took place in the Department of Cardiovascular Surgery, Shanghai Jiao Tong University Affiliated First People's Hospital, Shanghai, China, between January 2000 and July 2008. Five hundred and ninety-three elderly patients (age ≥70-years-old), undergoing isolated CABG were retrospectively divided into diabetic group and non-diabetic group. We analyzed the pre-operative, intra-operative, and post-operative variables of the 2 groups. The t-test, Chi-square test, and multivariate logistic regression were used to determine the differences between the 2 groups of patients.

Results: There was no statistical difference of pre-operative and intraoperative variables between the 2 groups, except that there were more left main coronary artery diseases in the diabetic group. Values in the post-operative period such as morbidity, complications, and blood infusion had no differences between the 2 groups. Diabetes mellitus and age are not the risk factors for in-hospital mortality.

Conclusions: Coronary artery bypass grafting in elderly patients is plausible. Furthermore, diabetic patients could get the same surgical results as those non-diabetic patients.

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With the improvement of living condition and medical science, there were more elderly patients with chronic diseases, such as diabetes mellitus (DM) and coronary artery disease. Also, with the improvement of percutaneous coronary intervention (PCI), patients undergoing coronary artery bypass grafting (CABG) were more serious. Bardakci et al[1] reported that both in-hospital mortality rate and postoperation morbidity rate were significantly higher among octogenarians who underwent CABG. The discharging rates for

octogenarians were significantly lower. However, after propensity matched comparison, Mamoun et al[2] suggested that older and younger patients had similar mortality and morbidity after CABG, despite that there were some complications in the older patients. Also, it has been known that coronary artery disease patients with DM had more severe lesions and more complications than those without DM. The prognosis of diabetic patients was rather poor than that of non-diabetic patients, no matter CABG[3] or PCI[4] was performed. Recently, some researchers[5,6] reported that diabetic patients underwent CABG could get similar low early mortality and morbidity, compared to non-diabetic patients. Hence, diabetes is not a risk factor for in-hospital mortality following CABG. High glucose was considered to interfere the function of neutrophils and promote the expression of proinflammatory factors, which might increase the incidence of post-operation complications. Accordingly, hyperglycemia contributes to the early postoperation mortality and morbidity. Thus, we considered that the effect of diabetes on the early outcomes of CABG may be due to the badly control of blood glucose level. Meantime, whether aged patients with diabetes could get the same post-CABG outcome as non-diabetic aged patients is not clear. In this study, we sought to study the early outcomes of 30 days post-operation in aged diabetic patients undergoing CABG in terms of early mortality and morbidities.

Methods. We retrospectively analyzed 593 elderly patients (≥70-years-old) undergoing isolated CABG in the Department of Cardiovascular Surgery, Shanghai Jiao Tong University Affiliated First People's Hospital, Shanghai, China, between January 2000 and July 2008. After the approval from the hospital research and ethical committee, the medical records of all patients, who were admitted with the diagnosis of coronary artery disease, were retrieved from the electronic database. All patients undergoing primary isolated CABG were included and those who had CABG combined with other heart operations or redo-CABG were excluded. We grouped the patients into diabetic group and non-diabetic group according to the pre-operative diagnosis. There was no statistical difference between the pre-operation variables, except who had some degree of left main disease in the diabetic group (**Table 1**).

The set of study endpoints was referred to published article and as follows:[7] The primary study endpoints were in-hospital mortality, defined as all cause of death within 30 days after surgery or during the same time period of hospitalization as well as postoperative major adverse cardiac events (MACE) during the period of hospitalization including perioperative myocardial infarction (PMI) or low cardiac output syndrome (LCOS). Secondary study endpoints were the composite study endpoints death or PMI and death or PMI or LCOS as well as other postoperative complications such as stroke or minor adverse events like new-onset ventricular arrythmia, major bleeding, necessity for rethoracotomy or postoperative renal failure requiring temporary hemodialysis. The standard for CABG was at least one stenosis ≥70% on angiography. Diabetes mellitus was defined as those requiring treatment with nutritional modification, oral medications, and/or insulin at the time of surgery. Renal insufficiency was defined as creatinine >120 μmol/L and no dialysis dependency. Chronic pulmonary obstructive disease (COPD) was defined as patient requires pharmacologic therapy for the treatment of chronic pulmonary compromise, or patient with an Forced expiratory volume in one second (FEV1) <75% of predicted value. Peripheral vascular disease (PVD) was defined as claudication either with exertion or at rest, absence of pedal pulses, and/or ischemic ulcers, amputation for arterial insufficiency; aorto-iliac occlusive disease reconstruction; peripheral vascular bypass surgery, angioplasty or stent; documented abdominal aorta aneurysm, repair or stent; or non-invasive carotid test with >75% occlusion. Cerebrovascular disease (CVD) was defined as unresponsive coma >24 hours, cerebrovascular accident (CVA), or transient ischemia attach (TIA). Cerebrovascular accident was defined as global or focal neurological deficit lasting less (transient ischemic attack) or more than 24 hours (reversible ischemic neurologic deficit; stroke). Mediastinitis was defined as at least one of the following: (1) an organism isolated from culture of mediastinal tissue or fluid; (2) evidence of mediastinitis seen during operation; (3) one of the following conditions: chest pain, sternal instability, or fever (>38.8°C), in combination with either purulent discharge from the mediastinum or an organism isolated from blood culture or culture of mediastinal drainage. Myocardial infarction was defined as new Q-wave postoperatively in 2 or more contiguous leads of the ECG. Vasoactive agent support was defined as the use of one or more vasoactive agents for any length of time. Postoperative LCOS was supposed to be present with a cardiac index below 2.0 L/min/m^2 or a systolic arterial pressure below 90 mm Hg, despite high-dose inotropic support (intravenous: dopamine ≥10 μg/kg/minute or dobutamine ≥10 μg/kg/minute or epinephrine >0.3 μg/kg/minute) with or without the use of an intra aortic

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balloon pump (IABP). Through a median sternotomy, 40% (n=237) of procedures were performed without the use of cardiopulmonary bypass (CPB). Internal mammary artery, radial artery, right gastro-omental artery and great saphenous vein were harvested as bridge materials. Blood glucose was monitored and controlled under 10.0 mmol/L by insulin. In CPB group, antegrade perfusion of cold blood crystal cardioplegia was adopted. The anastomoses were performed in the following sequence: right coronary artery (RCA), left circumflex artery (LCX), diagonal artery (Diag), and left anterior descending coronary artery (LAD). The proximal anastomoses were constructed under cardiac blockade. Perfusion pressure was maintained at 80 mm Hg, thus, as to maintain cerebral and renal perfusion. In non-CPB group, after systematic heparinization (1 mg/kg), activated clotting time was maintained >300s, and a mechanical heart stabilizer (Octopus II-III Medtronic, MN, USA) was used to facilitate distal anastomosis. A side-biting clamp was applied in proximal anastomosis. There was no statistical difference of operative materials between the 2 groups (**Table 1**).

Fluid (Ringers lactate 100 ml) was administrated if cardiac index (CI) was ≤2.0 L/min/m^2 and/or mean arterial pressure (MAP) <70 mm Hg and dopamine (start with 5 μg/kg/minute), if adequate response to fluid was not obtained. Dobutamine starting with 3 μg/kg/minute or epinephrine starting with 0.1 μg/kg/minute was administrated if CI was ≤2.0 L/minute/m^2 and/or MAP <7 0mm Hg, while dopamine was administrated with 10 μg/kg/min. Intra-aortic balloon pump should be inserted if CI was ≤2.0 L/min/m^2 and/or MAP <70 mm Hg, while dopamine administrated with 10 μg/kg/min combining with dobutamine 10 μg/kg/min or epinephrine 0.3 μg/kg/min. The intravenous insulin therapy or subcutaneous insulin therapy was adopted to control blood glucose under 10.0 mmol/L. Given that blood glucose was controlled well, subcutaneous insulin therapy was adopted and monitor interval was prolonged 48 hours after surgery.

Numerical variables are presented as mean±SD, categorical variables are represented as the percentage of the sample. Stata 10.0 was adopted for statistical

Table 1 - Patients' demographics.

Patients' demographics.	Diabtetic group (n=180)	Non-diabetic group (n=413)	*P*-value
Gender (female)	62 (34.4)	118 (28.6)	0.15
Mean age (years)	74.8 ± 3.7	75.0 ± 3.7	0.43
Body mass index (kg/m^2)	24.0 ± 2.9	24.5 ± 3.1	0.10
Cardiac functional grading (III-IV)	48 (26. 7)	101 (24.5)	0.57
CCS function class (III-IV)	121 (67.2)	283 (68.5)	0.75
Extent of coronary artery disease			
1 vessel	11 (6.1)	36 (8.7)	
2 vessel	27 (15.0)	66 (16.0)	0.51
3 vessel	142 (78.9)	311 (75.3)	
Left main coronary artery lesions	81 (45.0)	146 (35.4)	0.03
Previous percutaneous coronary intervention	18 (10.0)	32 (7.8)	0.36
Ejection fraction (%)	57.4 ± 9.5	58.7 ± 10.0	0.14
Previous myocardial infarction	43 (23.9)	117 (28.3)	0.26
Hypertension	123 (68.3)	252 (61.0)	0.09
Chronic pulmonary obstructive disease	12 (6.7)	21 (5.1)	0.44
Cerebrovascular disease	5 (2.8)	22 (5.3)	0.17
Renal insufficiency	1 (0.6)	3 (0.7)	0.82
Peripheral vascular disease	7 (3.9)	9 (2.2)	0.24
Emergent surgery	2 (1.1)	9 (2.8)	0.37
On-pump procedures	111 (61.7)	245 (59.3)	0.59
Mean cardiopulmonary bypass time (min)	115.5 ± 34.7	118.1 ± 34.9	0.51
Mean aortic cross-clamp time (min)	85.1 ± 26.5	86.5 ± 28.0	0.66
Distal anastomosis	3.0 ± 0.9	2.9 ± 1.0	0.08
Use of Internal mammary artery	153 (85.0)	332 (80.4)	0.18
Re-operation for bleeding	3 (1.7)	19 (4.6)	0.08

CCS function class - Canadian Cardiovascular Society function class for angina

Table 2 - Post-operation materials of the 2 groups.

Post-operation materials	Diabetic group (n=180)	Non-diabetic group (n=413)	*P*-value
Death	10 (5.6)	19 (4.6)	0.62
Vaso-active agent maintenance	36 (20.0)	105 (25.4)	0.15
Intra-aortic balloon pumping	3 (1.7)	4 (1.0)	0.47
Drainage	580.47 ± 424.0	586.09 ± 542.9	0.90
Blood transfusion	161 (89.4)	350 (84.8)	0.13
Complications			
Atrial arrhythmia	11 (6.1)	19 (4.6)	0.44
Respiratory cardiac arrest	1 (0.6)	1 (0.2)	0.54
Malignant arrhythmia	1 (0.6)	2 (0.5)	0.90
Peri-operative MI	0 (0)	1 (0.2)	0.51
Low cardiac output syndrome	5 (2.8)	13 (3.2)	0.81
Renal insufficiency	3 (1.7)	4 (1.0)	0.47
Pleural effusion	6 (3.3)	12 (2.9)	0.78
Pulmonary infection	1 (0.6)	5 (1.2)	0.47
Incision infection	1 (0.6)	2 (0.5)	0.90
Mediastinitis	0 (0)	1 (0.2)	0.51
Sternum dehiscence	0 (0)	2 (0.5)	0.35
Pulmonary embolism	0 (0)	2 (0.5)	0.35
Cerebrovascular accident	1 (0.6)	2 (0.5)	0.90
Alimentary tract hemorrhage	0 (0)	1 (0.2)	0.51
Multiple organ failure	0 (0)	2 (0.5)	0.35

Table 3 - Risk factors of operative mortality in multivariate analysis.

Variable	Odds ratio	*P*-value	95% (confidence intervals)
Diabetes mellitus	0.82	0.66	0.34 - 1.99
Cardiac functional grading	0.34	0.003	0.16 - 0.69
Age	0.90	0.05	0.81 - 1.00
Chronic pulmonary obstructive disease	0.29	0.05	0.08 - 1.01
Peripheral vascular disease	0.07	0.000	0.02 - 0.24
Cerebrovascular disease	2.10	0.51	0.24 - 18.59
Hypertension	1.36	0.48	0.58 - 3.19
Renal failure	4.16	0.53	0.05 - 360.17
Myocardia infarction history	1.41	0.49	0.53 - 3.78
Emergent surgery	0.09	0.004	0.02 - 0.45
Re-operation for bleeding	0.16	0.01	0.04 - 0.67

analysis. The t test and x^2-test were used to determine the differences in patient's characteristics for numerical variables and categorical variables. Multivariate logistic regression was used to assess the risk factors of early mortality. A p-value of <0.05 was considered significant for all tests.

Results. There was no statistical difference of the operative variables between the 2 groups, though there was more patients were re-operated for bleeding in the non-diabetic group. Main complications after operation were hemorrhage, atrial fibrillation, pleural effusion and LCOS. Furthermore, there was no statistical difference of the mortality and morbidities between the 2 groups (**Table 2**). Twenty-nine patients died in both groups. The main death were respiratory cardiac arrest, low cardiac output syndrome, malignant arrhythmia, pulmonary embolism, respiratory failure, CVA and multiple organ failure. One hundred and forty-one patients needed post-operation vasoactive agent maintenance (**Table 2**). A multivariate analysis was performed in the relations between the operative mortality and the variables pre- and intra-operation which were the significant contributory risk factors in univariate analyses. Diabetes mellitus, hypertension, MI history and CVD were assigned to multivariate analysis compulsorily. Diabetic mellitus was not a risk factor for early mortality. Cardiac functional grading, PVD, emergency operation and re-operation for bleeding were the significant risk factors (**Table 3**).

Discussion. Parallel with the increasing of life expectancy of Chinese people, which was 73 years in 2005,[8] and it will be 81 years in 2050, there will be more and more aged patients with DM. Accordingly, the number of aged patients undergoing CABG due to severe atherosclerotic disease has been increasing over the years.[1] Octogenarians generally manifested a higher incidence of preoperative risk factors and postoperative complications, hospital stay, and in-hospital mortality rate were significantly among octogenarians higher than those among younger patients.[1] However, Mamoun et al[2] compared the patients undergoing CABG and found that patients aged 85 years and older and patients aged 55-65 years who underwent CABG had similar mortality and morbidity, except that older patients had more blood transfusion and atrial arrhythmias morbidity. As our opinion, aged patients may have more complications, but the early outcome of surgery is similar to young patients (data not shown). In this old aged patients analysis, age is not the independent risk factor for peri-operative mortality either.

In this study, the total mortality was 4.9%, diabetic

patients had more mortality than that of non-diabetic patients, but there was no difference (5.6% versus 4.6%, p=0.62). The data of Bardakci et al[1] in 37 hospitals showed that mortality in patients over 65-years-old was 3.08%. The mortality in patients over 85-years-old was 3.3%.[2] Ishikawa et al[9] reported a total mortality of 4% in a study of 1973 patients over 70-year-old, the mortality of diabetic patients was 6.44% in their study. All these data show that aged diabetic patients may have similar operative mortality as other patients. Diabetes mellitus was considered to be an independent risk factor for cardiovascular events. Patients with diabetes more frequently have left main coronary artery lesions, multi-vessel disease, and diffuse CAD.[10-12] Similarly, there were also more left main coronary artery lesions in diabetic patients in this study. Though there was no statistical difference, there were more hypertension patients in diabetic group. Moreno et al[13] reported that diabetic patients have a larger amount of lipid-rich plaques, which may be more prone to rupture. Sequentially, CABG surgery was associated with less MACE and is superior to PCI.[14] Disadvantages related to hyperglycemia may be resulted from some mechanisms as follows: 1) Tissue damage. Hyperglycemia may inhibit the activity of glucose-6-phosphate dehydrogenase (G6PD), leading to acutely superoxide production of activated neutrofils; increase the potentiality of infection.[14] Hyperglycemia can induce the transcriptional regulation of inflammatory and pathologic genes as well as their receptors via specific signaling pathways, resulting in increased monocyte activation, migration, and adhesion to the endothelium. Also, it can induce the expression of atherogenic genes. All these inflammation and atherogenic genes activation lead to tissues damage and pathogenesis of atherogenesis pre- and post-surgery.[16] Furthermore, diabetes contributes to platelet dysfunction enhancing platelet adhesiveness and hyperaggregability, potentiating coronary thrombosis.[17,18] 2) Impairment of energy metabolism. Hyperglycemia may represent a state of insulin resistance and impairment of signaling to the target organs.[19] Release of catecholamines and cortisol and other stess hormones increases due to the body's stress response during surgery, which may worsen insulin resistance. Inhibition of glycolysis results in an increased concentration of free fatty acid and a decrease of myocardial glucose uptake, which leads to a decreased production of adenosine triphosphate (ATP).[20] In line with Antunes'[6] results, our data show no statistical difference of early mortality and morbidity between the diabetic and non-diabetic groups, which indicates diabetic patients could get the same early surgery outcome as non-diabetic patients. From the materials we found that mortality and morbidity decreased as time pass by, with the level of blood glucose was controlled more strictly (data not shown). We recommend that blood glucose level be monitored every 2 hours during the first 48 hours after the operation and insulin must be used to control the blood glucose level <10.0 mmol/L. To those severe patients, insulin pump is recommended. If the blood glucose level is controlled well, subcutaneous insulin is used and monitor interval is prolonged in the rest time during the hospital stay. Oral medication or insulin is given after the patients discharge from the hospital. Doenst et al[21] and Jones et al[22] et al reported that hyperglycemia during cardiopulmonary bypass and post-operation predicts mortality in patients undergoing cardiac surgery. The mortality dropped with blood glucose controlled. We consider that DM might affect the progress of coronary artery lesion and prognoses of CABG. However, the adverse effects of diabetes decrease with minor operation damage, shorter operation time, and CPB time, especially the strict control of the level of blood glucose peri-operation. Only pre- and intra-operative variables were analyzed, so the patients' risk and operation deciding could be estimated before the surgery. Peripheral vascular disease, cardiac functional grading, emergent operation and re-operation were found to be contributory risk factors for in-hospital death by Logistic regression. In line with our results, PVD, poor left ventricular function and emergent operation were reported as significant contributory risk factors to operative death.[9,23] Patients with these conditions should be estimated and prepared strictly before operation, so as to reduce the potential operative complications and mortality. However, COPD was found not to be a risk factor in aged CABG patients, which was different from others.[1] There were also some limitations of the study. First, it was the experience of single medical center and it was a retrospective one. Second, there was no age stratification in the study, and there might be some differences between septuagenarian and octogenarian. Third, due to serum markers of MI were not routinely carried out in our center, the judgement of MI was defined as Q wave on ECG manifestation, which might neglect non Q wave MIs. However, the early outcome of serum markers for MI could be affected by cardiac operation. Hence, we might seek for better way to diagnose post-CABG MI.

In summary, CABG may have an accepted outcome, though there are some risk factors for in-hospital death. With strictly glucose control, DM is not a risk factor anymore. As for aged patients, with satisfying control of blood glucose, they could receive the same satisfying early surgery outcome as non-diabetic patients.

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Related topics

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