Effect of Lower-Extremity Bypass Surgery on Inflammatory and Endothelium marker in Diabetic Patients

Pei-Hsuan Tsai[1], Yu-Chen Hou[1] , Yao-Chung Chang[2] , Sung-Ling Yeh[1]
[1] Institute of Nutrition and Health Sciences, Taipei Medical University, Taipei, Taiwan
[2] Department of General Surgery, Taipei Medical University-Wan Fang Hospital, Taipei, Taiwan

Introduction

Diabetic ulcers are the most common foot injury leads to lower extremity amputation in Diabetes Mellitus (DM) patients underwent lower-extremity bypass surgery (LEBS). LEBS may increase perfusion and blood flow to tissues and prevent amputation of the extremities. This study investigated the inflammatory and endothelium markers before and after LEBS to understand the alterations of ischemia-reperfusion on tissue in DM patients with LEBS. Since endothelin-1(ET-1) and nitric oxide (NO) correlated with normalization of vascular function, blood lactate levels during cardiopulmonary bypass are often used to verify adequacy of perfusion. Plasma ET-1, NO and lactate levels were measured. Also, inflammatory-related mediators were analyzed in this study.

Subjects and Methods

Twenty-one type 2 DM patients with LEBS were included and thirteen varicose vein bypass subjects were treated as control. Blood was drawn before and at 1 and 7 d after surgery in DM patients and 1 d postoperatively in control subjects. Plasma ET-1 and NO as well as inflammatory related markers including soluble intercellular adhesion molecule (sICAM), soluble vascular cell adhesion molucule (sVCAM), C-reactive protein (CRP) were analysis by ELISA kits. Plasma lactate levels were measured by colorimetric method. Leukocyte integrin (CD11a/CD18 and CD11b/CD18) expressions were measured by flow cytometry.

Results and discussion

The results showed that there were no significant differences in plasma ET-1, lactate and NO levels before and after LEBS in DM patients, nor did any difference in ET-1, lactate and NO concentrations were observed between the DM and the control subjects before and 1d after surgery. We analyzed lymphocyte CD11a/CD18 because CD11a is the only integrin expressed by lymphocytes. Previous studies showed that alloantigen-induced lymphocyte proliferation, T-cell-mediated cytotoxicity, and B-cell immunoglobin production were CD11a/CD18-dependent. In this study we found that lymphocyte CD11a/CD18 expressions were higher on postoperative 1d in control patients than those in DM patients, suggesting that lymphocyte CD11a/CD18 expressions were suppressed in DM patients. Compared with the control group, plasma sVCAM, sICAM and CRP levels increased in DM group. However, no differences in these markers before and after LEBS in DM patients. These results suggest that chronic inflammation existed in DM patients, and LEBS did not alleviate the inflammatory condition.

Conclusion

This study demonstrated for the first time that compared with the varicose vein bypass subjects, DM patients had higher plasma sVCAM, sICAM and CRP levels and lymphocyte CD11a/CD18 expressions were suppressed. Since there were no differences in concentrations of ET-1, NO and inflammatory mediators in DM patients before and after LEBS, it seemed that the effect of LEBS on alleviating the inflammatory condition and endothelial dysfunction was obscure.

References

1. El-Mesallamy, H., Suwailem, S., and Hamdy, N. (2007). Evaluation of C Reactive Protein, Endothelin-1, Adhesion Molecule(s), and Lipids as Inflammatory Markers in Type 2 Diabetes Mellitus Patients. Mediat Inflamm *2007*, 1-7.
2. Matsumoto, K., Sera, Y., Abe, Y., Tominaga, T., Horikami, K., Hirao, K., Ueki, Y., and Miyake, S. (2002). High serum concentrations of soluble E-selectin correlate with obesity but not fat distribution in patients with type 2 diabetes mellitus. Metab Clin Exp *51*, 932-934.

Table 1
Characteristics of the subjects[1,2]

	Diabetes	Control	*P* value
Case No.	21	13	
Age, y	70.7 ± 9.0	67.5 ± 12.0	0.396
Sex M/F	10/11	2/11	
BS, mg/dl	175.9 ± 59.5	109.6 ± 34.1*	0.002
HbA1C, %	8.7 ± 2.3	--	
Total cholesterol (mg/dl)	152.9 ± 35.6	185.0 ± 44.5*	0.0319
HDL-C, mg/dl	32.7 ± 13.1	53.9 ± 17.8*	0.0013
LDL-C, mg/dl	86.0 ± 33.2	110.0 ± 37.3	0.1706
TG, mg/dl	145.8 ± 81.6	122.1 ± 100.8	0.4718
CRE, mg/dl	3.70 ± 3.44	1.12 ± 1.16	0.0159

[1]BS, blood sugar；HbA_1C, hemoglobin A_1C；HDL-C, high density lipoprotein cholesterol；LDL-C, low density lipoprotein cholesterol；TG, triglyceride; CRE, creatinine.
[2]Data are expressed as mean ± SD.* significantly different between the 2 groups

Table 2
Plasma endothelin-1(ET-1), lactate, nitric oxide (NO) Concentrations in the subjects before and after surgery[1]

Day	ET-1 (pg/mL)	lactate (mmol/L)	NO (μ mol/L)
Diabetes			
0	2.2 ± 0.5	2.2 ± 1.0	3.5 ± 1.7
1	2.0 ± 0.2	2.2 ± 0.7	2.5 ± 0.7
7	2.2 ± 0.4	2.1 ± 0.9	3.4 ± 1.9
Control			
0	2.1 ± 0.4	2.6 ± 2.1	3.1 ± 1.6
1	2.0 ± 0.2	2.1 ± 0.4	2.3 ± 1.0

[1] Data are expressed as mean ± SD

Table 3
Expressions of lymphocyte CD11a/CD18 and neutrophil CD11b/CD18 in the subjects before and after surgery[1]

Day	CD11a/CD18 (%)	CD11b/CD18 (%)
Diabetes		
0	48.2 ± 18.0	3.1 ± 2.0
1	42.4 ± 12.0	2.9 ± 1.3
7	43.5 ± 12.3	3.5 ± 1.1
Control		
0	48.0 ± 20.3	3.8 ± 1.6
1	52.5 ± 12.2*	3.6 ± 1.4

[1] Data are expressed as mean ± SD
* Significantly different from the d 1 of diabetes group

Table 4
Plasma intercellular adhesion molecule (ICAM), vascular cell adhesion molucule (VCAM) and C-reactive protein (CRP) Concentrations in the subjects before and after surgery[1]

Day	VCAM	ICAM (ng/mL)	CRP
Diabetes			
0	1406.2 ± 839.7	344.3 ± 121.8	53.4 ± 46.7
1	1415.9 ± 722.6	332.3 ± 112.1	64.6 ± 54.9
7	1224.9 ± 632.8	398.5 ± 126.9	48.3 ± 45.7
Control			
0	588.1 ± 314.5*	224.2 ± 55.1*	1.3 ± 1.2*
1	533.2 ± 162.0†	230.3 ± 58.0†	3.9 ± 3.3†‡

[1] Data are expressed as mean ± SD.
* Significantly different from d 0 of the diabetes group.
+ Significantly different from d 1 of diabetes group.
‡Significantly different from d 0 of control group.