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Hemodynamic Effects of the Geometric Dimensions of Graft Vessels in Coronary Artery Bypass Graft Models

The objectives of this investigation are to evaluate the rheologic properties in atherosclerotic disease treated with the various coronary artery bypass graft (CABG) models by numerical analysis, we used four different CABG models for the assessment of spatial fluctuation in wall shear stress, pressure variation and mass flow rate with Carreau model and Navier-Stokes equation. Wall shear stress was higher in a naturally tapered model (model 1) and a constant (non-tapered) diameter of the graft vessel the same as the distal LAD (model 4) than in others. Pressure variation along the native coronary artery and graft vessels was higher in a model 4, model 1 than in a reverse tapering model (model 2) and a constant diameter of the graft vessel the same as the proximal LAD (model 3). The mass flow rate of the distal part (kg/sec, $\dot{m}_o$) was the highest in model 3. This study suggests that in vitro spatial simulation following CABG revealed that small caliber or tapered graft vessels have adverse hemodynamic effects on the native and graft vessels. By this technique it is possible to simulate the optimal distribution of local hemodynamic variables in patients treated with CABG, also to minimize the degeneration of graft vessel.

Key Words : *Coronary artery bypass; Hemodynamics; Investigative technique, numerical analysis*

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INTRODUCTION

The initial process of atherosclerosis is a response to injury to the endothelium and smooth muscle cells of the vascular wall and consists of the formation of fibro-fatty and fibrous lesions, preceded or accompanied by the vascular inflammatory reaction. Furthermore, when advanced, these become the disease and may occlude the involved artery and result from an excessive inflammatory fibroproliferative response to numerous different forms of injury (1). In addition to this biologic aspect, biomechanics-related factors such as wall shear stress, pressure change and turbulent flow also play a role in the development and the progression of coronary atherosclerosis (2).

Coronary artery bypass graft (CABG) operation has been one of the widely performing treatment modalities for coronary artery obstructive disease. However, degenerative change and occlusion of the graft vessels or stenosis of the anastomosis site have been another serious problems following the CABG (3). There is a lack of information regarding the spatial distribution of local hemodynamic changes following the CABG. This may play a role in the development of atherosclerosis in the graft and native vessels. Numerical analysis with computed simulation is a useful in vitro technique that allows the spatial distribution of local hemodynamic variables of native and grafted vessels.

This study was designed to test the hypothesis that local hemodynamic variables of the native and grafted artery are different according to the different CABG models. Present study is probably the first study to define the geometric and hemodynamic variation using a computed simulation and human in vivo hemodynamic parameters. To accomplish this aim, we visualized geometric pattern and quantitated the wall shear stress, pressure variation and mass flow rate in the four common different CABG models.

MATERIALS AND METHODS

CABG models

To evaluate the hemodynamic simulation in the four different graft models, the basic CABG models were

adopted from a human angiogram of the left internal mammary artery (LIMA) grafted to left anterior descending (LAD) coronary artery (Fig. 1A). Native coronary and left internal mammary angiogram were performed by the femoral approach according to standard techniques. For computed simulation, measured diameter of LIMA using a quantitative coronary assessment (QCA system, Philips Integris 3000, Netherland) were converted to ratio of native coronary artery reference diameter. And we also performed the promising new techniques involving two-dimensional intracoronary ultrasound (Fig. 1B) for measuring the percent luminal stenosis, vessel wall thickenss in the stenotic area of the native coronary artery and grafted vessel and also coronary flow measurement using intracoronary Doppler wire, proximal and distal to the stenotic lesion, and grafted LIMA flow velocity (Fig. 1C). This basic model (Fig. 2) allowed to input in vivo hemodynamic data and the vascular structural parameter.

1) The coronary artery had 70% fixed stenosis of 2 mm length and its diameter tapered from proximal (Di) to distal (Do, Do=0.7×Di) approaching total length of 25 mm.
2) The graft vessel was end to side anastomosed at the site just below the stenotic portion, the angle of anastomosis was 60°.
3) Finally, we set the four different CABG models according to the diameter changes of proximal and distal portion of graft vessel (di → do). Model 1: a naturally tapered model (di=Di, do=Do), model 2: a reverse tapering model (di=Do, do=Di), model 3: a constant (non-tapered) diameter of the graft vessel the same as the proximal portion of LAD (Di) and model 4: the constant diameter of the graft vessel the same as the distal portion of LAD (Do) (Table 1).

Rheologic properties of blood

Considering the human blood as the non-Newtonian viscosity, so we used constitutive equation that represents the apparent viscosity of blood as a function of shear rate. Among various constitutive equations, we used the Carreau model of following equation to specify the shear rate versus apparent viscosity relationship.

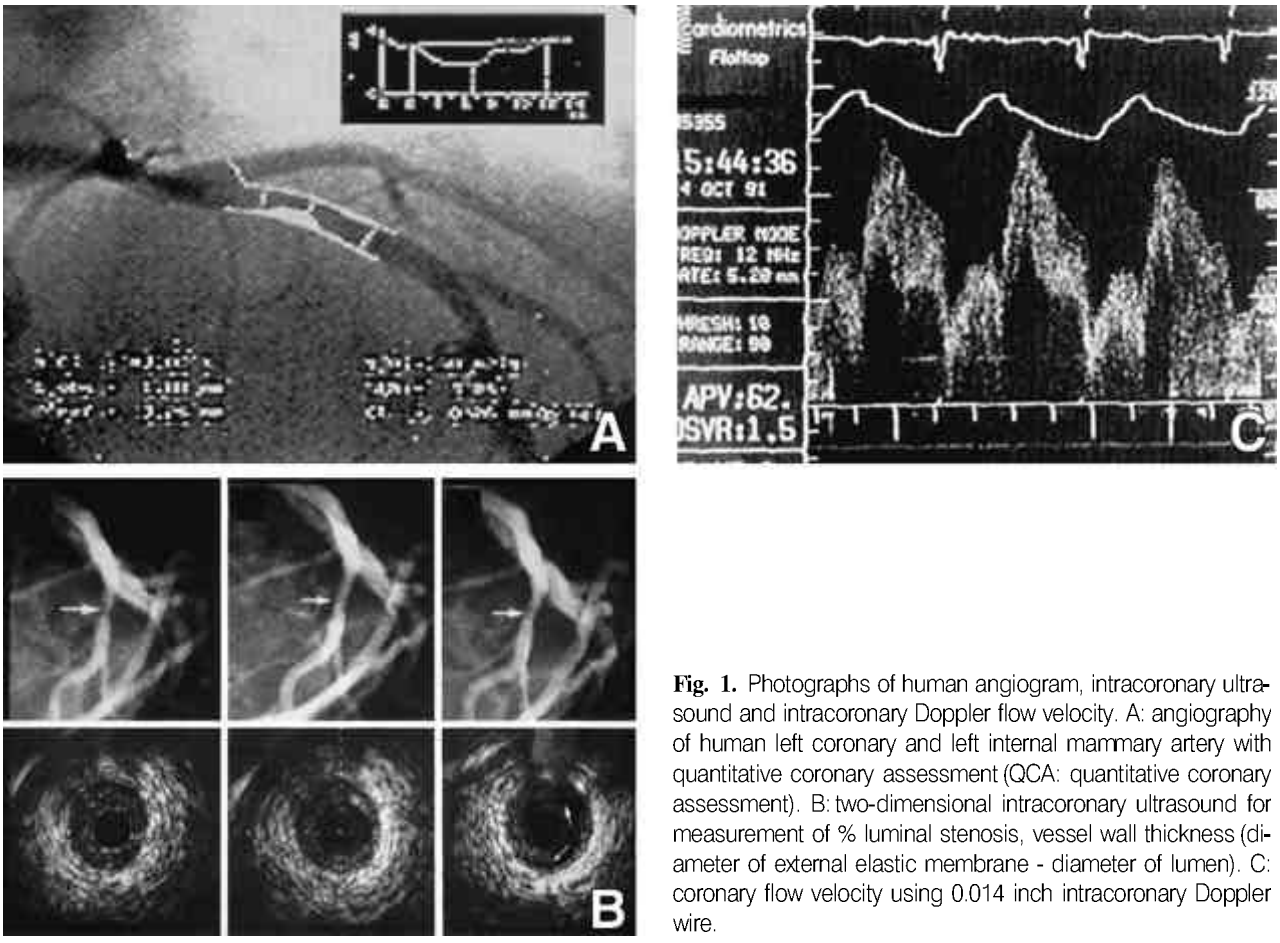

Fig. 1. Photographs of human angiogram, intracoronary ultrasound and intracoronary Doppler flow velocity. A: angiography of human left coronary and left internal mammary artery with quantitative coronary assessment (QCA: quantitative coronary assessment). B: two-dimensional intracoronary ultrasound for measurement of % luminal stenosis, vessel wall thickness (diameter of external elastic membrane - diameter of lumen). C: coronary flow velocity using 0.014 inch intracoronary Doppler wire.

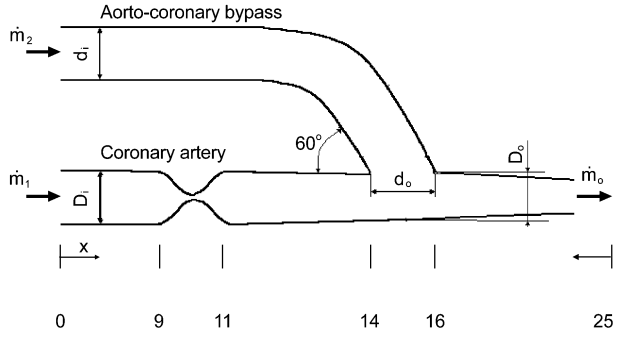

Fig. 2. CABG model according to geometric dimension. The native coronary artery has 70% fixed stenosis of 2 mm length (9-11) and its diameter tapered from proximal(Di) to distal(Do, Do=0.7×Di) approaching total length of 25 mm. And 3 mm below the stenotic portion, graft vessel is end to side anastomosed (14-16), the angle degree of anastomosis is 60°.

$$\eta=\eta_\infty+(\eta_0-\eta_\infty)[1+(\lambda\dot{\gamma})^2]^{\frac{(q-1)}{2}}$$

(η_0, η_∞: apparent viscosity at zero-shear rate and infinite-shear rate; λ: elapsed time; q: constants)

Once the local shear rate is attained, the apparent viscosity of blood can be determined by this equation.

Governing equations

Carreau model and the Navier-Stokes equation were used to specify the shear rate versus apparent viscosity relationship and to calculate hemodynamic variables. The tensor form of the governing equation to analyze the steady flow hemodynamic of native coronary artery and the graft vessels is as follows (5, 6, 7).

$$\frac{\partial u_j}{\partial x_j}=0 \quad (1) \qquad \rho u_j\frac{\partial u_i}{\partial x_j}=-\frac{\partial p}{\partial x_i}+\frac{\partial \tau_{ij}}{\partial x_j} \quad (2)$$

$$\tau_{ij}=\eta\left(\frac{\partial u_i}{\partial x_j}+\frac{\partial u_j}{\partial x_i}\right) \quad (3)$$

(u_j: velocity vector, p: pressure, ρ: density, τ_{ij}: wall shear tensor, η: constant of viscosity)

Distributions of velocity, pressure variation, and shear stress of the vessel wall are obtained by solving the governing equation.

Numerical analysis

To attain a effective numerical analysis of the hemodynamics we used the infinite volume method, hybrid difference scheme and Simple-C scheme via SUN SPARC workstation 20 (AEA Co., New England). As described above, we used in vivo flow-velocity of the native left coronary artery and internal mammary artery.

Table 1. Various geometric dimensions of graft vessels

	d_i	do
Model 1	D_i	D_o
Model 2	D_o	D_i
Model 3	D_i	D_i
Model 4	D_o	D_o

Four different CABG models according to the diameter changes of proximal and distal portions of graft vessel(di → do). Model 1: a naturally tapered model(di=Di, do=Do), Model 2: a reverse tapering model(di=Do, do=Di), Model 3: a constant(non-tapered) diameter of the graft vessel the same as the proximal portion of LAD(Di), Model 4: the constant diameter of the graft vessel the same as the distal portion of LAD(Do), Do=0.7×Di

After visually determining the geometric pattern of the four basic models, the following hemodynamic variables were calculated 1) wall shear stress: force per unit area of vessel wall (τ), 2) pressure variation: pressure changes along the native and grafted artery, 3) mass flow rate: distal blood flow per second supplying myocardium (mass flow rate, $\dot{m}_o$, kg/sec) from the concept of impedence (stenotic portion) which suggested that a large amount of blood flow was supplied to a low impedence area.

RESULTS

The effects of the various geometric dimensions on the hemodynamics of CABG models are as follows;

1. wall shear stress of the stenotic portion (model 1= model 4 > model 2 > model 3) and anastomosis site of the graft vessel (model 4 > model 1 > model 2 > model 3) were different (Fig. 3).
2. recirculation areas (turbulent flow areas) were present at the inner, outer wall of the distal portion of the stenosed native coronary artery and the outer wall of the graft vessel (portion just distal of the anastomosis site) (Fig. 3).
3. the pressure variations of proximal part of the anastomosis site of native coronary artery and graft vessels were different (model 4 > model 1 > model 2 > model 3) (Fig. 4).
4. the mass flow rate of the distal part (kg/sec, $\dot{m}_o$) was the highest in model 3 (model 1: 0.003560, model 2: 0.003700, model 3: 0.003904, model 4: 0.003551) (Table 2).

DISCUSSION

This study was designed to investigate the biomechan-

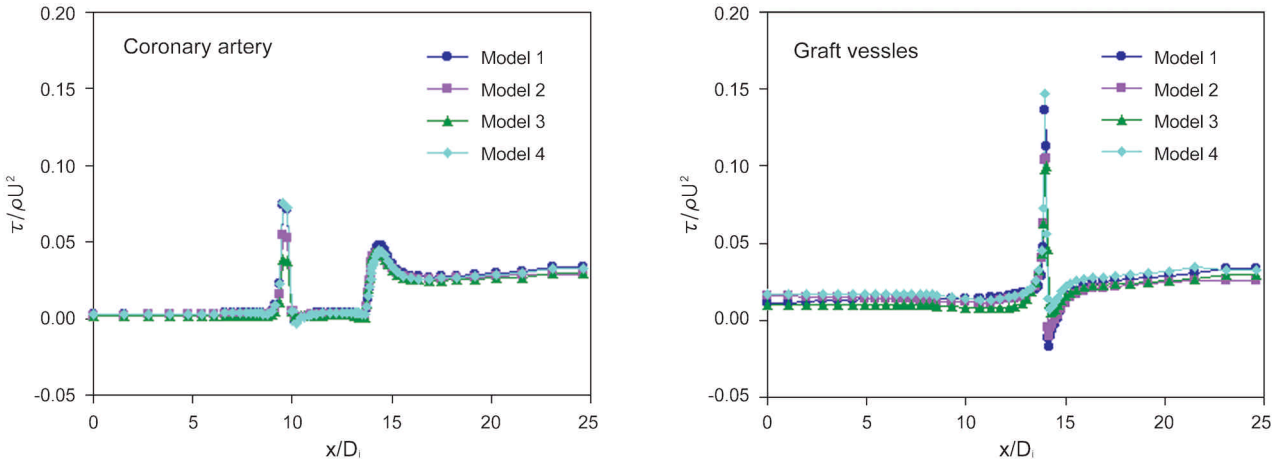

Fig. 3. Shear stress along the outer wall of coronary artery and inner wall of graft vessels. X: distance of CABG model as Fig. 2. Y: wall shear stress(τ): force per unit area of vessel wall

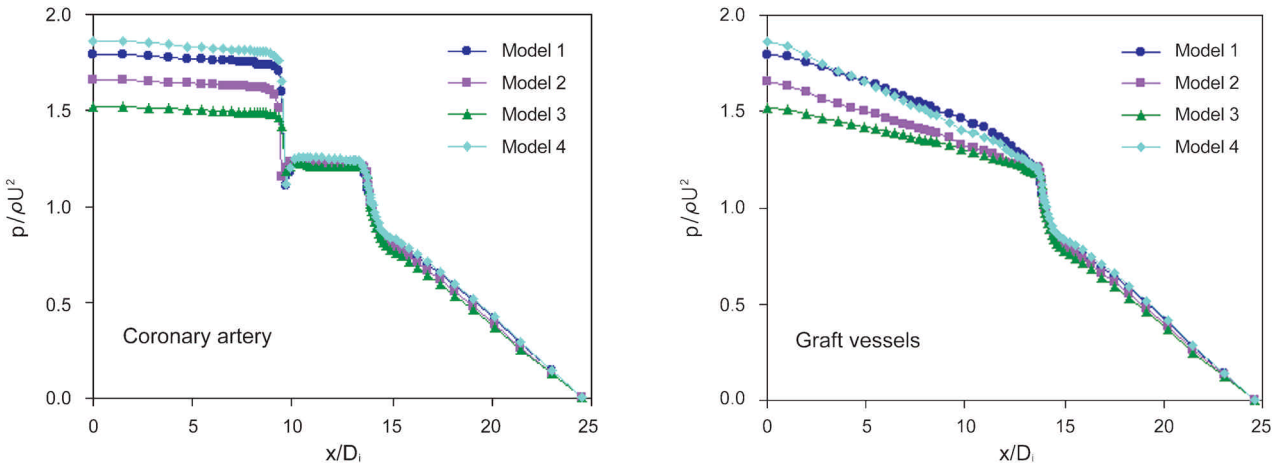

Fig. 4. Pressure variations along the coronary artery and graft vessels. X: distance of CABG model as Fig. 2. Y: pressure variation(p): pressure changes along the vessels

Tabe 2. Mass flow rate of various CABG models

	$\dot{m}_1$	$\dot{m}_2$	$\dot{m}_o$
model 1	0.000466	0.003094	0.003560
model 2	0.000376	0.003324	0.003700
model 3	0.000304	0.003600	0.003904
model 4	0.000481	0.003050	0.003551

Mass flow rate: blood flow supplying myocardium (mass flow rate, kg/sec) from the concept of impedence (stenotic portion) which suggests that a large amount of blood flow is supplied to a low impedence area.
$\dot{m}_1$: input mass flow rate to native coronary artery
$\dot{m}_2$: input mass flow rate to graft vessel
$\dot{m}_o$: output(distal) mass flow rate supplying myocardium

ical patterns of the coronary-grafted vessels according to the four different CABG models. There were significant differences in wall shear stress, pressure variation and mass flow rate according to the characteristics of the four different models. Wall shear stress of the stenotic portion of the native artery was higher in model 1 and model 4 than in others, and that of the anastomosis site of the graft vessel was the highest in model 4. Pressure variation along the native coronary artery and graft vessels was higher in a constant (non-tapered) diameter of the graft vessel the same as the distal LAD (model 4) and a naturally tapered model (model 1) than in a reverse tapering model (model 2) and a constant diameter of the graft vessel the same as the proximal LAD (model 3).

The mass flow rate of the distal part (kg/sec, $\dot{m}_o$) was the highest in model 3. Present study of in vitro spatial simulation following CABG suggests that small caliber or tapered diameter of graft vessels has adverse hemodynamic effects such as wall shear stress and pressure variation on the native and the graft vessels.

After the first introduction of the coronary artery bypass graft (CABG) operation (12) as a surgical revascularization, it is still the most commonly used surgical treatment modality for coronary artery obstructive disease worldwide. However, the high occlusion rate of graft vessels in long-term follow up is one of the most common disappointing limitations (3). To improve graft patency, there have been continuous investigations in the fields of surgical technique, vascular biology, and biomechanical research (4). In the biologic aspects of graft vessels, cell to cell interaction, humoral stimuli of cytokines and bacterial products such as gram-negative endotoxins which act directly on cultured human endothelial cells to alter their adhesive properties for blood leukocytes, are known to play important roles in the progression of obstructive lesions (8). In addition to this biochemical paradigm of endothelial activation, endothelial cells also are constantly exposed to a spectrum of hemodynamic forces such as wall shear stress, hydrostatic pressure, pulsatile flow velocity. When cultured endothelial cells are exposed to hemodynamic forces, a spectrum of structural and functional changes is observed, i.e., changes in cell shape, cell alignment and cytoskeletal architecture, membrane deformability and cell division rate (8).

When the native artery, which is distal to the stenotic lesion, is bypassed with a vein graft, formation of the recirculation (turbulent flow) and flow stagnation occur in the part just distal to the stenotic native vessel. These hemodynamic changes might precipitate the transportation of low density lipoprotein cholesterol (LDL cholesterol) and retention of LDL at the vascular wall, as well as adhesion of monocytes which plays a role in the development of medial smooth muscle cell activation and intimal hyperplasia (9). Arterial bifurcation and curvatures, where disturbed flow patterns occur, are known to be the prevalent sites of the intimal hyperplasia, whereas geometries associated with uniform laminar flow and relatively constant wall shear stress, such as the straight tubular portions of the aorta and its branching vessels, tend to be lesion-protected areas (8). In this study, the recirculation areas were present at the outer wall of the distal part of the anastomosis site, so late graft occlusion might easily occur in this area. The important factors in graft vessels occlusion after CABG are wall shear stress, difference in flow velocity and diameter mismatch of graft vesseles and native artery (10). Among these factors, low and/or oscillating shear stress impairs the vascular endothelial cell function and promotes atherosclerotic change (10). In addition to this factor, pressure change caused by turbulent flow may weaken the atheromatous plaque and fasten plaque tearing. We knew that the highest wall shear stress occurred just distal to the stenotic portion, and low shear stress at the recirculation area (Fig. 3). The wall shear stress of the stenotic portion (native coronary artery) and anastomosis site (graft vessel) was the highest in model 4 and lowest in model 3 (model 4 > model 1 > model 2 > model 3). It is better to avoid models 4 & 1 to minimize recirculation area and maintain constant wall shear stress. In the area of high shear stress, high density red blood cells expells the low density platelet to the periphery, so platelet-rich white thrombus may be frequently found in severe stenotic portions and fibrin-rich red thrombus in recirculation areas (13). Smooth muscle cell and endothelial cells are important sources of heparan sulfate which is known to inhibit smooth muscle cell proliferation. So decreased wall shear stress due to the hemodynamics of the recirculation area may inhibit heparan sulfate production, activate smooth muscle cell proliferation and promote atherosclerosis (11). A recent study has revealed that endothelial dependent relaxing factor (EDRF) and prostacyclin also act to maintain constant coronary vessel tone (14). In the point of diameter changes of graft vessel (Table 1), the pressure variations of proximal part of the anastomosis site of native coronary artery and graft vessels in model 2 (reverse tapering, Do → Di) and model 3 (large non-tapered diameter, Di → Di) are relatively small compared to those in model 1 (naturally tapering, Di → Do) and model 4 (small diameter Do → Do) but distal to the anastomosis site that is almost the same in all models (Fig. 4). This result may come from the flow competition between the native coronary artery and the graft vessels. We also assessed the amount of distal blood flow supplying myocardium (mass flow rate, $\dot{m}_o$, kg/sec) from the concept of impedence (stenotic portion) which suggested that a large amount of blood flow was supplied to a low impedence area. The result was that the largest amount of blood was perfused in model 3 (Table 2).

A central premise of modern vascular biology is that the endothelial lining is a dynamically mutable interface, locally responsive to various stimuli originating from the circulating blood (non-Newtonian fluid) and/or neighboring cells and tissue, and thus can actively participate in the physiologic adaptation or pathophysiologic dysfunction of a given region of the vasculature. This adaptation process involves various adhesive mechanisms. For example, real-time visualization of a cultured endothelial monolayer exposed to a unidirectional laminar shear stress stimulus reveals a dynamic remodelling of the focal

contact sites along its basal aspect (8). Changes also are observed in the phosphorylation state of cytoskeletal proteins associated with these focal adhesion complex, as well as adhesion molecules such as platelet-endothelial adhesion molecule-1 that are localized to lateral cell-cell junctions (2). These changes presumably are part of a generalized cellular adaptation to applied mechanical stresses. Present study suggested that simulated hemodynamic variables using a human in vivo hemodynamic and vascular structural parameters were different between the models. This will be helpful to tailor the optimal CABG models to improve graft vessel patency and longevity.

However we had some limitations in practically applying this results to clinical settings. And there is marked individual variation in vascular structure and hemodynamics such as diameter mismatch between native coronary artery and left internal mammary artery, setting graft vessels as conduits only without considering the molecular biologic factor, the vascular compliance, and elasticity of the vessel wall.

Further studies under the various conditions in vitro and in vivo biologic studies will be needed.

REFERENCES

1. Ross R. *The pathogenesis of atherosclerosis: a perspective for the 1990s. Nature 1993; 362: 801-9.*
2. Konstantopoulos K, Mclntire LV. *Effects of fluid dynamic forces in vascular cell adhesion. J Clin Invest 1996; 98: 2661-5.*
3. Bourassa MG. *Long-term vein graft patency. Curr Opin Cardiol 1994; 9: 685-91.*
4. Loop FD. *Internal-thoracic-artery graft-biologically better coronary arteries. N Engl J Med 1996; 334: 263-7.*
5. Suh SH, Roh HW, Yoo SS, Kwon HM. *Numerical simulation of blood flow in the human left coronary artery. The 9th Int. Symp. on Trans. Phenomena in the Thermal-Fluids Eng 1996: 91-6.*
6. Hong SK. *Mechanical factors in the pathogenesis, localization and evolution atherosclerosis. Workshop on the Biomechanical Fluid Dynamics, AFERC, POSTECH, 1993: 21-2.*
7. Biro GP. *Comparison of acute cardiovascular effects and oxygen supply following haemodilution with dextran, stroma-free haemoglobin solution and fluorocarbon suspension. Cardiovasc Res 1982; 16: 194-204.*
8. Gimbrone MA, Nagel T, Topper JN. *Biomechanical activation: an emerging paradigm in endothelial adhesion biology. J Clin Invest 1997; 99: 1809-12.*
9. Berliner JA, Navab M, Fogelman AM, Frank JS, Demer LL, Edwards PA, Waston AD, Luis AJ. *Atherosclerosis: basic mechanisms oxidation, inflammation, and genetics. Circulation 1995; 91: 2488-96.*
10. Falk E, Shah PK, Fuster V. *Coronary plaque disruption. Circulation 1995; 92: 651-71.*
11. Libby P. *Molecular bases of the acute coronary syndromes. Circulation 1995; 91: 2844-50.*
12. Favaloro RG. *Saphenous vein autograft replacement of severe segmental coronary artery occlusion: operative technique. Ann Thorac Surg 1968; 5: 334-47.*
13. Sherman CT, Litvack F, Grundfest W, Lee M, Hickey A, Chaux A, Kass R, Blanche C, Matolff J, Morgenstern L, Ganz W, Swan HJC, Forrester J. *Coronary angioscopy in patients with unstable angina pectoris. N Engl J Med 1986; 315: 913-9.*
14. Mehta JL, Nicolini FA, Donnelly WH, Nichols WW. *Platelet-leukocyte-endothelial interactions in coronary artery disease. Am J Cardiol 1992; 69: 8B-13B.*