

## The effect of competitive flow on both the flow and the velocity in venous grafts in a bypass model

*Baypas modelinde yarışmalı akımın venöz greftlerdeki akım ve velosite üzerine etkisi*

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### ABSTRACT

**Objective:** The term “competitive flow” defines the flow from a partially stenosed native artery that “competes” with the flow from a graft to perfuse the distal tissues. The purpose of our study is to investigate the effects of competitive flow at different degrees of stenosis at common carotid artery, in a rabbit model by measuring both the flow volume and velocity in the venous graft.

**Methods:** This prospective experimental study included 33 rabbits, which were divided into three groups: in Group 1, the common carotid arteries were ligated to form a total occlusion, in Group 2, the common carotid arteries were externally incompletely ligated to achieve 50% stenosis, and in Group 3, common carotid arteries were fully patent. The jugular vein was reversed and anastomosed to proximal and distal common carotid arteries using end to side anastomosis technique. Mean arterial pressure, the total flow and velocity were measured in native carotid arteries prior to surgery and in venous grafts 2 months after surgery using Doppler ultrasonography. Statistical analysis was performed using Chi-square test and Kruskal Wallis analysis of variances.

**Results:** There were no differences in graft mean velocity (Group 1 - 16.8±6.7 cm/sec, Group 2 - 14.1±6.1 cm/sec and Group 3 - 12.1±6.7 cm/sec), and mean flow volume (Group 1 - 33.9±11.5 mL/min, Group 2 - 29.0±8.3 mL/min, and Group 3 - 24.4±12.8 mL/min) between groups after surgery (p>0.05 for both).

**Conclusion:** As it was the case in this rabbit model, the reduction of flow volume or velocity in lesser degrees of stenosis in the carotid artery venous bypass grafts is not significant in a statistical perspective. Although in short-term this effect did not create a difference for graft patencies between the groups, it may be important in long-term (*Anadolu Kardiyol Derg 2009; 9: 123-7*)

**Key words:** Competitive flow, vein graft, bypass, arterial occlusion

### ÖZET

**Amaç:** Yarışmalı akım, kısmen tıkalı olan nativ arterdeki akımın greftteki akımla distal perfüzyon için yarışması olarak tanımlanır. Bu çalışmanın amacı karotis arterde değişik oranlarda darlık oluşturulan tavşan modelinde venöz greftlerde velosite ve volüm miktarını ölçerek yarışmalı akımın etkisini araştırmaktır.

**Yöntemler:** Bu deneysel prospektif çalışmada 33 tavşan üç gruba ayrıldı. Grup 1’de kommon karotis arter total olarak bağlandı. Grup 2’de karotis arter %50 darlık meydana gelecek şekilde daraltılırken Grup 3’te arter tamamen açık bırakıldı. Juguler ven çevrilerek “end-to-side” tekniikle kommon karotis arterin distal ve proksimaline anastomoz edildi. Hemodinamik değerlendirme amacıyla, cerrahi girişimden önce ve 2 ay sonra karotis arterlerde ortalama kan basıncı, total akım hacmi ve akım hızı ölçümleri Doppler ultrasonografi ile yapıldı. İstatistiksel analizde gruplardaki veriler Ki-kare ve Kruskal Wallis varyans analiz testleri ile değerlendirildi.

**Bulgular:** Venöz greftlerdeki ortalama akım hızı (Grup 1 - 16.8±6.7 cm/sn, Grup 2 - 14.1±6.1 cm/sn ve Grup 3 - 12.1±6.7 cm/sn) ve akım volümü (Grup 1 - 33.9±11.5 mL/dk, Grup 2 - 29.0±8.3 mL/dk, Grup 3 - 24.4±12.8 mL/dk) istatistiksel olarak grup 1, 2 ve 3 arasında farklı değildi (p>0.05).

**Sonuç:** Oluşturulan tavşan modelinde, darlık oranlarının az olduğu karotis arterlere uygulanan venöz baypas greftlerinde, volüm ve hız azalması istatistiksel olarak anlamlı tespit edilmedi. Her ne kadar kısa dönemde gruplar arasında kompetitif akımın etkisi anlamlı bulunmasa da uzun dönemde önemli olabilir. (*Anadolu Kardiyol Derg 2009; 9: 123-7*)

**Anahtar kelimeler:** Yarışmalı akım, venöz greft, baypas, arteriyel darlık

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## Introduction

The term "competitive flow" defines the flow from a partially stenosed native artery that "competes" with the flow from a graft to perfuse the distal tissues. It is suggested that, in coronary arteries where a critical stenosis is not present, one of the major reasons for inadequacies and the progression of occlusion after the bypass with the arterial grafts is due to the competitive flow in the coronary artery (1, 2). The relationship regarding postoperative inadequacies or occlusions of saphenous vein grafts with the degree of stenosis in the native coronary arteries is not clear. Some researchers suggest that, when the stenosis is not critical (under 70%) in the coronary artery, reduction in the patency of the saphenous vein grafts is observed (1-5).

On the other hand, in some reports it was suggested that the competitive flow only affects the arterial grafts and but not the patency in the saphenous vein grafts (6, 7). Actually, this is still a matter of debate. Similarly, the effect of competitive flow on the bypass grafts in the uncritical stenosis of peripheral arterial diseases has not been evaluated yet.

The purpose of our study was to investigate the effects of the competitive flow, by measuring both the volume and velocity in the jugular vein bypass grafts, placed in the carotid artery of rabbits with varying degrees of stenosis or occlusions created.

## Methods

This prospective experimental study was performed with the cooperation of Cardiovascular Surgery and Radiology departments of the Medical Faculty at the Surgical Research Centre of our University between the dates December 15<sup>th</sup>, 2005 and December 15<sup>th</sup>, 2006. Approval from the Local Animal Studies Ethics committee was obtained prior to the study.

A total of 33 New Zealand white rabbits, with an approximate weight around 2 to 3 kilograms, were used for the study. All animals received humane care during the study period. Anesthetic induction was achieved with intramuscular administration of 50 mg/kg of ketamine hydrochloride and 2ml/kg of xylazine hydrochloride. The neck regions of each rabbit had been shaved. Before the initiation of surgery, the suitability of both carotid artery and the jugular vein were evaluated, using 14 mHz Doppler ultrasonographic probe (Toshiba Aplio 80, SSA-770A, 2004, Japan). Special care was given to ensure that the carotid artery had no stenosis and the jugular vein had adequate diameter. In all groups, for physiologic and hemodynamic evaluation, the total flow and velocity of native carotid arteries were measured with the Doppler ultrasonography (USG) before arteriotomy. The jugular veins of the subjects were between 2.5 to 3.5 mm millimeters in diameter (mean:  $2.93 \pm 0.57$  mm). Heparin administration (150 IU/kg) via jugular vein during the subcutaneous phase of preparation, prior to anastomosis was done for all the subjects. Cefazolin-Na (10ml/kg) was used intramuscularly for antimicrobial prophylaxis. Local papaverine injections to perivascular areas were applied to achieve

vasodilatation. Initially the common carotid artery had been exposed, and the segment between the origin and the internal carotid bifurcation was occluded with microvascular clamps. According to study protocol, for rabbits in group 1, carotid artery was ligated totally with a 4/0 silk suture (a complete occlusion). In group 2, under the vision of a surgical microscope, a stenosis of 50% was created with 10/0 polypropylene sutures. The stenosis created was evaluated with Doppler USG intraoperatively at this phase and an estimation was made. For those, stenosis between 40% to 70% percent, the narrowing was considered to be 50% on average. In cases where this cannot be achieved, sutures were removed and replaced to form the aimed degree of stenosis, and evaluated again with Doppler USG. In group 3, the carotid arteries were left intact and completely patent. With the use of microscopes, a segment of ipsilateral external jugular vein, 3 cm's in length, were excised in all the rabbits. These pieces of jugular veins were placed in warm saline solution. For the anastomosis in the proximal and distal part of the common carotid artery a 1 mm arteriotomies were performed. The jugular veins were reversed and anastomosed to proximal and distal common carotid arteries using an 8/0 polypropylene suture with end-to-side and continuous fashion (Fig. 1). After the completion of both anastomosis, clamps were released. The flow in the vein grafts and arteries were then evaluated with Doppler USG (Fig. 2). Surgery was completed after meticulous hemostasis and all the surgical layers were closed. The subjects were controlled throughout the daily visits. At postoperative 1st and 4th weeks, the surgical site was evaluated with Doppler USG and those with early total occlusion (either the artery or the venous graft) were excluded from the study with the thought of technical surgical error. At postoperative 2<sup>nd</sup> month under general sedation with halved doses of initial anesthetic agents, a Doppler USG was conducted. The total flow volume and velocity in the venous grafts (systolic and diastolic) were measured with the Doppler USG. Before the venous graft measurements, mean arterial pressures were recorded in all three groups for hemodynamic evaluation.

### Statistical analysis

The data were evaluated through the SSPS 10.0 statistical software. The continuous data from each of the three groups were compared using Kruskal Wallis analysis of variance. Patency and stenosis rate following surgery were assessed using Chi-Square test. Values of p less than 0.05 were considered significant.

## Results

The results of the total flow and velocity in native carotid arteries prior to surgery are shown in Table 1. Statistically, the differences between group 1, group 2 and group 3 were not significant ( $p > 0.05$ ). Eight of the subjects were excluded from the study after the evaluations at 1st and 4<sup>th</sup> postoperative weeks, due to complete thrombotic occlusion of vein grafts in 6 animals and anastomotic high degree stenosis in 2 animals (Table 2).

These events were accepted to be due to inconvenient surgical techniques. Patency and stenosis rate following surgery were not significantly different between three groups ( $p < 0.05$ ). At postoperative 2<sup>nd</sup> month, mean arterial pressure, both the velocity and flow volumes at systolic and diastolic phases, in the venous grafts of the remaining 25 subjects were measured. There were no significant differences between 3 groups in terms of mean arterial pressure and Doppler USG parameters (all  $p > 0.05$ ) (Table 3).

### Discussion

In this study, the competitive flow in the native artery serving as a contributing factor to the possible inadequacies in the venous graft was not found to be valid. There were no differences in mean velocity and mean flow volume in the grafts between studied groups with varying degrees of stenosis.

It is widely accepted that the most common causes for the inadequate flow rates during the early postoperative days following the application of the arterial and the venous grafts in the coronary artery bypass graft (CABG) surgery are due to physiologic (vasospasm, pressure, vessel runoff) or technical reasons such as (anastomotic quality, twists or kinks in the graft). It is also suggested that the competitive flow is another eluding aspect. When the stenosis is not critical in the native

**Table 1. Preoperative mean velocity, flow and pressure measurements in native carotid artery**

Variables	Group 1 (n=11)	Group 2 (n=10)	Group 3 (n=12)	p*
Mean velocity, cm/sec	14.0±3.0	17.3±4.0	16.2±4.6	0.138
Mean flow, ml	25.8±6.1	23.4±5.4	24.8±11.00	0.469
Mean arterial pressure, mmHg	71.7±6.7	68.7±5.7	66.6±5.5	0.132

Data are presented as mean±SD  
\*Kruskal Wallis analysis of variance

**Table 2. Patency and stenosis rate in venous grafts in studied groups**

Variables	Group 1 (n=11)	Group 2 (n=10)	Group 3 (n=12)	p*
Patent grafts, n	9	7	9	0.817
Stenotic graft, n	2	3	3	

Data are presented as proportions  
\*Chi-square test

**Table 3. Doppler and hemodynamic variables two months after surgery**

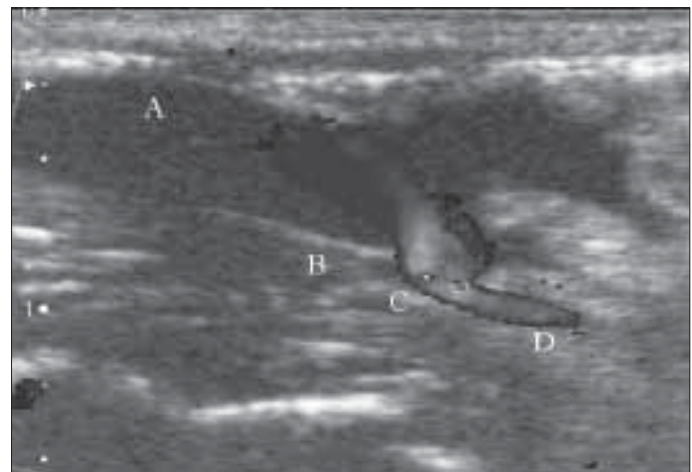
Variables	Group 1 (n=9)	Group 2 (n=7)	Group 3 (n=9)	p*
Mean velocity, cm/sec	16.8±6.7	14.1±6.1	12.1±6.7	0.165
Mean flow, ml/min	33.9±11.5	29.0±8.3	24.4±12.8	0.141
Mean arterial pressure, mmHg	74.5±4.7	68.4±5.5	66.2±5.8	0.139

Data are presented as mean±SD  
\*Kruskal Wallis analysis of variance



**Figure 1. An image of completed anastomosis of jugular vein graft to common carotid artery.**

A - proximal carotid artery, B - carotid artery between two anastomosis, C - jugular vein graft, D - distal carotid artery



**Figure 2. The Doppler ultrasonographic image of venous graft and artery anastomosis.**

A - jugular vein graft, B - carotid artery before anastomosis site, C - anastomosis site, D - carotid artery after anastomosis site

artery, the native artery flow may compete with the flow in the graft causing a reduction in the volume of flow and the resultant inadequacies (1-4, 8).

The internal thoracic artery (ITA) distal occlusion is a common phenomenon after the ITA left anterior descending artery (LAD) bypass surgery. It is asserted that such obstruction is associated with the flow dynamics and the variations in the pressure. In the cases where less than 50% of stenosis is present in the native coronary artery, it is argued that, developments of stenosis (narrowing) occur in the distal part of ITA (9). Shimizu et al. (1) have measured velocity, volume flow and diameter in ITA by dividing the bypass patients between the ITA and LAD in accordance with their levels of stenosis in LAD of > 80%, 60-79% and 40- 59%. As a result of their study, it is asserted that, the flow in the case of native artery where there are no critical stenosis, as a result of competition in the flow of the ITA, causes a decrease in the levels of velocity, volume flow

and reduction in the diameter of the ITA graft and thus inadequacies in the graft and the development of atrophy are suggested (1). In contrast, a different study indicated that, there was not relationship between the ratio of narrowness in the native coronary artery and the ITA patency. However, when the stenosis is not critical in the native artery, the diameter of the ITA graft is reduced over time (10).

Generally, bypass or interventional treatments are conducted for coronary and peripheral arterial disease with critical stenosis. In our study, to represent cases with critical stenosis up to total occlusion requiring treatment, totally ligated carotid artery model (described as Group 1) with a bypass conduit served for evaluation. Those for having less critical stenosis with controversial competitive flow phenomenon were evaluated in group 2. In group 3 completely patent carotid artery and bypass graft actually served as the controls for comparisons. The total flow and velocity in native carotid arteries were measured with the Doppler US before starting surgical intervention. We wanted to see the effect of physiological factors and the relationship between native carotid arteries and venous graft measurements. There were no any differences between groups. Also, mean arterial pressures of the subjects were recorded and statistically there were not any variation in three groups. Inconvenient surgical techniques cause graft failure in a few weeks following surgery. Failure was detected in eight of the grafts after the evaluations at 1st and 4th postoperative weeks. We thought there were technical problems with these 8 grafts and excluded them from the study. Only full patent grafts were included in to the study.

Otaki et al. (11) in a study with dogs, after ligating the circumflex artery on the beating heart, had individually anastomosed ITA and saphenous vein grafts to distal circumflex artery separately. In the acute phase a reduction in the flow of the ITA and no change in the flow regarding the vein graft were observed. However, during the chronic phase, through a series of angiographies they observed that the ITA's were occluded (clogged) one by one but the saphenous veins retained their patencies. It was emphasized that when the flow in the ITA is thought to be insufficient the additionally placed venous grafts carried out the essential function and the occlusion occurred over time in the ITA (11). It was also underlined, according to the findings of this study, that the venous grafts were not affected by the competitive flow formed by the native artery. Our study findings regarding the venous grafts are much similar to those of Otaki et al. (11). In our study, venous grafts were used for the purpose of bypass and results between the three groups regarding the difference of the velocity and the rate of volume flow in the vein grafts were not statistically significant. Therefore, mild or severe stenosis in the native artery will not be a determining factor for the intensity of the competition and the consequent inadequacies of the graft. Eight of the subjects were excluded from the study as a result of thrombotic occlusion or anastomotic high degree stenosis in grafts. Although the occlusion or stenosis in venous grafts could be due to competitive flow or to the development of intimal hyperplasia, we excluded

these subjects from the study in order to evaluate the velocities and flow volumes two months later.

In the earlier studies, it was shown that when the endothelial cells in the artery walls are subjected to newly formed different flow patterns, they are triggered to release vasoreactive mediators such as nitric oxide and prostaglandin. These mediators have relaxing effects on the smooth muscle cells, providing an adaptive period for the arterial bed to for accommodation to the new blood volume and/or to rate of flow (12, 13). It was also hypothesized that the retrograde systolic volume flow and the resulting oscillating flow pattern to the ITA from the native artery as a result of the competition injures the endothelium, triggering failure in the arteries adaptation mechanism against the new flow, resulting in inadequacy of ITA (9). Saphenous vein graft is actually a passive conduit and does not possess these adaptive mechanisms mentioned above. It is also known that the retrograde flows in the vein grafts are comparatively much less. Thus, it is less affected by the competitive flow generated in the native artery and therefore the inadequacies and the density of occlusions occurred much less in cases with less critical stenosis of the native artery (9). In our study, in group 3, native arteries were completely patent. Even though the flow volumes and velocities in the venous grafts were lower, the differences didn't reach to any statistically significant level, compared to other two groups. It can be speculated that, the reasons may be due to the passive nature of venous conduits which contributes to them, in being less affected from competitive flow.

The competitive flow can be observed after the coronary artery bypass surgery or interventions for peripheral arterial diseases. So far, most of the studies focused on the competitive flow after coronary bypass surgery and we have not encountered a study regarding the possible formation of competition in the bypass surgery for peripheral vascular occlusions. From this aspect, our study findings bear originality and probably will contribute to support of newer studies for coronary bypasses and peripheral artery surgery.

#### Limitations of the study

The number of animals in three groups were relatively low. Atherogenic regime could be used in animal models in order to make the study representative for human clinical situation. The time period of the study might be longer. Intimal and medial thickening in venous grafts might be detected by histopathological study.

#### Conclusion

As it was the case in this rabbit model, the reduction of flow volume or velocity in lesser degrees of stenosis in the carotid artery venous bypass grafts is not significant in a statistical perspective. Accordingly, the competitive flow in the native artery serving as a contributing factor to the possible inadequacies in the venous graft was not found to be valid. It is obvious that, further comprehensive and long-term studies either in human or animal subjects on competitive flow, are essential.

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