


Velocity Distribution and Intimal Proliferation in Autologous Vein Grafts in Dogs

STANLEY E. RITTGERS, PANAYOTIS E. KARAYANNACOS, JULIA F. GUY, ROBERT M. NEREM, GEORGE M. SHAW, JEPHRA R. HOSTETLER, AND JOHN S. VASKO

SUMMARY Autologous femoral veins grafted between the external iliac arteries in 18 dogs provided a model for studying the hemodynamics and histopathology of vein graft bypasses. The angle of proximal anastomosis was varied by groups (<90°, 90°, >90°) to produce a wide range of flow conditions within the grafts. Four months after implantation, point velocity measurements of blood flow and histological examination of the superior and inferior walls were made at proximal, middle, and distal locations in each graft. Hot-film velocity measurements revealed outwardly skewed velocity profiles in the proximal locations in all grafts, and flow visualization models showed secondary fluid motions and separation zones at those regions. Velocity profiles in the middle and distal regions of the grafts were more symmetrical and showed no flow separation. Histological examination of wall sections along the graft length showed that intimal proliferation occurred focally and ranged from 1 to 100 μm in thickness. No significant correlation between graft angle and degree of intimal proliferation was found. However, there was a weak inverse correlation between the apparent fluid shear rate and the corresponding degree of intimal proliferation, with the greatest proliferation occurring in the regions experiencing the lowest shear forces. Regions of low shear rate should be avoided by maintaining adequate flow rates through the grafts and thus minimizing losses of patency due to both thrombus formation and intimal proliferation.

HUMAN AORTOCORONARY saphenous vein bypass procedures are widely employed in the treatment of severe coronary artery disease. However, loss of graft patency has led to concern about the overall benefit of this procedure. Bypass failure rates of up to 23% during the first year have been attributed primarily to early occlusion (up to 1 month) by thrombosis or late occlusion (after 1 month) by intimal or subendothelial proliferation. Although its exact etiology is unknown, many investigators believe intimal proliferation to be a series of repairative

cine, Division of Cardiology, The Ohio State University, Columbus, Ohio 43212.

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processes in response to vein wall injury that results from
graft handling and preparations,6-8 distention of the graft
wall due to arterial pressure,9-15 ischemia resulting from
interruption or compression of the vasa vasorum9-15,16 and
other factors.18 Hemodynamic forces also may play an
important role in this process.11-13 and are of particular
interest because these forces can be controlled to some
extent by the bypass design. By analyzing both the fluid
velocity field and the local intimal proliferation within
grafts of various configurations, this study establishes a
significant relationship between hemodynamics and histo-
pathology in chronically implanted arterial vein grafts.

Methods

Surgical Preparation

Eighteen healthy foxhounds of either sex weighing 25-35
kg received autologous femoral vein bypass grafts
between the external iliac arteries. The dogs were divided
into three groups according to the angulation of the
proximal vein anastomosis (Fig. 1). Dogs in group I
received grafts at an acute angle (45° ± 10°) relative to
the proximal artery; group II, at a 90° ± 10° angle; and
group III, at an angle greater than 90° (125° ± 10°).

The dogs were premedicated with acepromazine (0.55
mg/kg) and atropine (0.05 mg/kg) 30 minutes before
operation. Anesthesia was initiated with sodium thiopen-
tal (20 mg/kg, iv) and maintained with a mixture of
nitrous oxide, halothane, and oxygen. An endotracheal
tube was placed and connected to a volume-controlled
respirator. After a low midline laparotomy, the retroperi-
toneal space was entered distal to the aortic bifurcation.
The external iliac arteries were mobilized and umbilical
tapes placed around them. A skin incision was made over
the right inguinal region and the femoral vein identi-
fied and mobilized over a length of 10 cm. The vein was
carefully dissected and tributaries were ligated with 6-0
polypropylene monofilament suture material. The section
of femoral vein was removed, carefully flushed with
heparinized saline at zero resistance, and placed in saline
at room temperature until the iliac arteries had been
prepared for anastomosis. Approximately 30 minutes
elapsed between the removal of the vein and the restora-
tion of blood flow through it.

After a segment of the right external iliac artery was
isolated between two atraumatic vascular clamps, a lon-
gitudinal arteriotomy was performed on the medial aspect
of the artery. An end-to-side anastomosis was performed
between the iliac artery and the distal end of the vein
graft, using a continuous suture with 6-0 polypropylene
monofilament. Upon completion of the anastomosis, the
graft was cross-clamped near the proximal end and flow
was restored through the right external iliac artery. The
graft was passed through a surgical opening in the meso-
rectum and brought into apposition with the left external
iliac artery, where a similar vascular anastomosis was
performed. All clamps were removed and the left external
iliac artery was twice ligated with 2-0 silk proximal to the
anastomotic site. As a consequence, blood flowing from
the right external iliac artery to the left external iliac
artery was now passing through the graft.

The mesorectum of all dogs was reconstructed with
interrupted 3-0 catgut sutures. The peritoneum was closed
with continuous 2-0 chronic catgut and the linea alba
apposed with interrupted 3-0 Dacron. Vetafil (Bengen
Co., W. Germany), a special veterinary suture material,
was used to close the skin. Both the distance between the
anastomotic sites and the aortic bifurcation and the shape
of the proximal and distal ends of the vein graft varied
depending on the angle between the proximal artery and
the graft. The dogs received antibiotic therapy with peni-
cillin and streptomycin for 1 week; sutures were removed
on the 10th postoperative day. Four months later, these
dogs were operated on again under similar anesthesia.
The abdominal aorta, external iliac arteries, and the vein
graft were dissected through a midline laparatomy.

**Figure 1** Experimental models with veins grafted between the external iliac arteries at proximal anastomoses of 45°, 90°, and 125°. The left external iliac artery is ligated proximal to the distal anastomosis in all groups.
Hemodynamic Measurements

When hemodynamic conditions had stabilized at the time of initial surgery, the external diameters of the iliac artery and of the proximal, middle, and distal locations of the vein graft were measured with a caliper. The true internal diameter was calculated by subtracting the thickness of the vessel from the caliper's reading. The length of the vein graft also was measured.

After the 4-month period of implantation, a lead from a standard electrocardiogram and blood velocities in the graft were recorded. Velocities were obtained by means of a hot-film anemometer system consisting of an in-house hot-film probe, a DISA 55D01 anemometer, and a DISA 55D10 linearizer (DISA Elektronik A/S, Denmark). The probe was constructed from an L-shaped 18-gauge needle by mounting a small platinum film-painted glass substrate on the needle tip. The probe tip was nominally 4 mm long and 1 mm thick, enabling measurements within 1 mm lamina. All velocity measurements with the hot-film anemometer system were taken with the probe maintained at a constant 2% temperature overheat (approximately 5°C) above the surrounding blood temperature. The principle of operation of hot-film anemometer systems and some of the problems encountered in their use in blood velocity measurements have been discussed elsewhere.19,21

Calibration of the system was accomplished by immersing the probe in an isotonic saline bath maintained near the dog's body temperature (38°C) by a thermostatically controlled water heater-circulator. The bath was contained in a circular channel mounted on a turntable so that the probe was exposed to a known, constant fluid velocity. The linearizer was adjusted so that anemometer signals for each probe followed a linear voltage-velocity relationship. It should be emphasized that the amount of heat released by the probe depends only on the velocity of fluid passing over it and not on the fluid direction.

In vivo velocity measurements within the graft were made by direct puncture of the vessel wall and insertion of the probe. Measurements were taken along the graft length at a position approximately 1 cm distal to the proximal anastomosis, at the middle of the graft, and at a position 1 cm proximal to the distal anastomosis. The probe was inserted in the plane of the graft anastomosis and for probe fouling due to fibrin deposition. When hemodynamic conditions had stabilized at the far wall and adding on the probe width. The probe was inserted in the plane of the graft anastomosis and for probe fouling due to fibrin deposition. When hemodynamic conditions had stabilized at the far wall and adding on the probe width.

The electrocardiogram was used as a time reference and simultaneous velocities at each position across the vessel lumen were recombined to form an entire velocity profile at a given graft location. Data reduction for this was accomplished with a Hewlett Packard 9830A computer, digitizer, and plotter system. Instantaneous velocity profiles at each quarter of the cardiac cycle and time-averaged velocity profiles representing the overall cardiac cycle were then obtained. Composite instantaneous and time-averaged velocity profiles were -derived at the proximal, middle, and distal locations of each angle group by averaging together the individual profiles of the six dogs in each group. This averaging consisted of normalizing each velocity profile to a unit area under the curve and then numerically averaging velocities point by point across the vessel diameter. This procedure was used to weigh each profile equally and thus provide an average shape of the group velocity profile. Apparent shear rates were calculated by dividing the velocity recorded nearest the graft wall by the 1-mm distance at which it was measured and assuming that blood velocity is zero at the wall. This is an approximation of the actual shear rate which is the slope of the velocity profile immediately at the wall (Fig. 2). Apparent shear rates were obtained at the superior and inferior wall segments of the proximal, middle, and distal locations of all animals. Group average apparent shear rates at each of the locations were derived from the apparent shear rates of the six dogs in each group.

Histological Measurements

On completion of the vein graft hemodynamic measurements, the descending aorta of each dog was perfused with 1 liter of normal saline followed by a solution of paraformaldehyde-glutaraldehyde in 0.1 M phosphate buffer, according to the fixation technique described by Karnovsky22 and modified by Hayat.59 Approximately 800–1200 ml of fixative were used over a 5- to 10-minute period to fix the vessel. Physiological pressure was main-

\[ \text{Blood Velocity, } u \]

\[ \text{Shear Stress} = \mu \frac{du}{dy} \text{ Wall} \]

\[ \mu = \text{Blood Viscosity} \]

\[ \left( \frac{du}{dy} \right) \text{ Wall} = \text{Shear Rate at the Wall} \]

**FIGURE 2** Relationship between blood velocity (u) and shear stress at the vessel wall. Fluid shear stress equals the slope of the velocity profile at the wall (slope of dashed line), or the shear rate \( \left( \frac{du}{dy} \right) \text{ Wall} \), times the coefficient of blood viscosity (\( \mu \)).
graded alcohols and propylene oxide before being placed in formalin and prepared for light microscopy. Tissues were osmium tetroxide for 2 hours, then processed through electron microscopy. These tissues were postfixed in 1% paraformaldehyde-glutaraldehyde solution. After 6 hours, they were washed in phosphate buffer and cut into superior, inferior, ventral, and dorsal longitudinal quadrants, according to their anatomical position in the graft site. The superior and inferior quadrants were cut into proximal, middle, and distal portions. Samples from the middle of each of these six vessel segments were prepared for electron microscopy. These tissues were postfixed in 1% osmium tetroxide and prepared for light microscopy. Tissues were washed, processed through graded alcohols and benzene, and embedded in Paraplast. Three sections from each segment were mounted on slides. Sections from the superior and inferior walls were examined using three histological stains (hematoxylin and eosin, Masson trichrome, and Verhoeff elastic-Mallory). Intimal thickness of each section was measured at three locations with a 400 mesh eye piece reticule calibrated in micrometers at 450 times magnification. Sections for electron microscopy were prepared on a Porter-Blum MT-2B ultramicrotome and mounted on 300 mesh copper grids. Sections were stained with uranyl acetate and lead citrate and observed with a Philips 300 electron microscope. To directly relate light microscopic observations to electron microscopic findings, thick sections (1μm) were prepared from each spurious-embedded specimen. These were stained with 1% methylene blue in 1% sodium borate solution and observed on the light microscope.

Statistical analysis of the histological measurements was performed using a multiple analysis of variance test, and the correlation analysis between apparent shear rates and intimal thickness measurements was performed by linear regression techniques. These tests were accomplished with statistical packages of the Hewlett Packard 9830A computer system.

Results

Hemodynamics

Internal graft diameters at the time of initial surgery averaged 7.5 ± 1.0 mm for the <90° group, 6.8 ± 1.7 mm for the 90° group, and 7.7 ± 0.8 mm for the >90° group. At the time of reoperation, internal graft diameters averaged 10.3 ± 0.8 mm for the <90° group, 10.3 ± 1.4 mm for the 90° group, and 11.7 ± 1.0 mm for the >90° group. This represents an overall average increase of 47% (P < 0.05) over the 4-month period.

Composite velocity profiles for each group are shown superimposed upon a schematic model. Peak velocities were 10.6, 10.9, and 11.4 cm/sec, respectively, with the velocity profiles being normalized with respect to each. Arrows indicate the direction of net blood flow, with lengths (L) and diameters (D) of all vessels drawn to scale. Average Reynolds number = 177.

arteries are drawn to scale. The figures clearly demonstrate consistently higher velocities near the inferior wall in the proximal location (1.0 ≤L/D ≤1.4) of all groups, with the greatest degree of skewing being in the 90° and >90° groups. This asymmetry of the velocity profile persists in the midgraft location (1.8 ≤L/D ≤2.2) of all groups, with the profile generally becoming more symmetrical at the distal location (2.7 ≤L/D ≤3.4). The length for establishment of a nearly symmetrical profile is again greatest in the 90° and >90° groups.

During the cardiac cycle, the velocity profiles fluctuated considerably, with the highest velocities and the most severe velocity profile skewing consistently occurring at three-quarters of a cardiac cycle following the R wave of the electrocardiogram in all groups. Lowest velocities and the least skewed velocity profiles generally occurred at one-half of the cardiac cycle. This variation is seen in detail in Table 1 which lists the minimum, maximum, and the time-averaged apparent shear rates acting on the various wall locations in each group. There is considerable fluctuation in apparent shear rates, with the maximum
value approaching six times the minimum value at some locations.

Histology

Light microscopic examination of all sections consistently demonstrated the presence of an intact endothelium (Fig. 6). Intimal proliferation was apparent in many grafts and consisted of increased smooth muscle cells, collagen fibers, and fibroblasts between the endothelium and the media. Measurements of intimal thickness were made by defining the intima as the region between the vessel lumen and the first circular smooth muscle layer of the media. Intimal thickness varied from section to section and ranged from 1 to 100 μm. The proliferation was not uniform but appeared in focal lesions (Fig. 7). The group-averaged intimal thickness of each of the graft locations was analyzed, and significant statistical differences between them were found. Figures 8-10 represent the average intimal thicknesses for the inferior and superior walls of the proximal, middle, and distal locations from each group. The intimal thickness of the superior wall is significantly greater than that of the inferior wall at the proximal location of all three groups (P <0.05). This is also seen at the distal location of the <90° group (P <0.05) and at the middle location of the 90° group (P <0.05). Intimal thickness tends to increase with distance along the inferior wall with the distal regions having thicker intima than the proximal regions in all three groups (P <0.05). There is no consistent location among all groups at which the greatest intimal proliferation occurs, nor is there an angle group in which intimal proliferation remains below the overall average of 8.02 μm at all locations. Moderate medial fibromuscular proliferation did occur in most areas of the grafts, but it did not correlate significantly with either intimal thickness or graft location.

Electron microscopy confirmed the presence of intact endothelium in all grafts. Figure 11 is an electron micrograph of a vein graft wall showing a normal ultrastructural morphology with typical intercellular material. Micrographs from other regions of the same and other grafts were similar in content except for differing degrees of intimal proliferation.

Finally, the average intimal thickness of each of the superior and inferior walls at the proximal, middle, and distal locations of all three groups was plotted vs. its corresponding apparent shear rate at 4 months. The resulting weak correlation (r = -0.201, P <0.10) shows an inverse dependence of intimal thickness on apparent shear rate, regardless of proximal angle, with the inferior walls generally experiencing lower intimal proliferation than the superior walls. Since the apparent shear rate is directly calculated from velocity near the wall, this may also be interpreted as an inverse correlation between average intimal thickness and velocity near the wall.

Discussion

The results of this study suggest that greater intimal proliferation occurs in regions exposed to relatively low shear rates in chronically implanted vein grafts. Intimal thickening does not depend directly on the angle of proximal anastomosis but is affected by the shearing forces produced within the graft.

A measure of the shear stress applied to a vessel wall by flowing blood may be obtained from velocity profiles, the detailed velocity data recorded at consecutive points across the lumen of a vessel (Fig. 2). Velocity profiles produced in vein grafts interposed with side-to-end anastomoses are asymmetrical proximally, regardless of the angle, due to the inertia of the fluid tending to resist any sudden change in flow direction. This is seen in all three experimental groups (Fig. 3-5), with the higher velocities occurring near the inferior wall and the lower velocities near the superior wall of the graft. The less skewed appearance of the velocity profile at the proximal location on the <90° group probably is due to the presence of significant circumferential and reverse secondary flows which are confirmed by in vitro flow visualization model experiments (unpublished observation). These motions are generated by the channelling of fluid against the inferior wall upon entering the graft, causing a separation region near the proximal superior wall and redirecting the flow circumferentially to create a spiral-like pathway.

**Table 1 Extreme Quarter Cycle and Time-Averaged Apparent Wall Shear Rates (sec⁻¹)**

<table>
<thead>
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<th></th>
<th>Proximal</th>
<th>Middle</th>
<th>Distal</th>
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<td></td>
<td>Sup</td>
<td>Inf</td>
<td>Sup</td>
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<td>&lt;90° Minimum</td>
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<tr>
<td>Average</td>
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<td>56</td>
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</tr>
</tbody>
</table>

Sup = superior wall; Inf = inferior wall.
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Kreid et al.25 have demonstrated similar flow disturbances within a “T” section model under conditions of steady flow. Since the hot-film anemometer does not have a direction sensing capability, as noted earlier, its output represents the resultant velocity at a given point. Thus, secondary motions, such as those present in the proximal region of the <90° group, cause additional heat loss from the probe and augment the velocity measurement at that location. Consequently, although the derived velocity profiles do not consist of forward velocities alone, they are indicative of the magnitude of the velocity at each point and thus, may be more informative as to the total shearing force acting on the wall.

The velocity profiles become nearly symmetrical within 3.5 diameters of the proximal anastomosis in all groups due to the viscous transfer of momentum between fluid layers. However, because of the increase in graft diameter of approximately 50% after 4 months, this length is 50% greater than that required for development of symmetrical flow in the grafts at the time of implantation. This enlargement exposes a significantly longer portion of the wall to both extreme high and low shear stresses and to potentially adverse fluid-wall interactions. Furthermore, the fluctuations seen in the velocity profiles during a cardiac cycle (Table 1) are also important since they imply a continuous cycling from high to low shear stresses acting on the wall.

The intimal proliferation observed in this study is consistent with results for both human and canine vein grafts reported elsewhere. Many studies indicate generalized hyperplasia of the subendothelial fibromuscular tissue which threatens the patency of the graft. Grondin et al.1 and Jones et al.26 both indicate patency-threatening generalized proliferation in human grafts. While the present data definitively document the occurrence of intimal thickening, the plaques found occurred in discrete locations and never compromised the vessel lumen. These focal sites of hyperplasia relate well to work done by Bond et al.,27 Brody et al.,9 and Vlodaver et al.7,28 Vlodaver's studies, however, suggest a much greater degree of intimal proliferation than that observed in our study. This variation may be due, at least in part, to differences between man and dogs. Faulkner et al.29 report opaque white intimal plaques similar to our observations, particularly in areas of increased peripheral resistance. All of these findings also agree with the present study in terms of histological composition.

Despite the focal occurrence of this proliferation, aver-
FIGURE 7 Low power light micrograph of vein graft wall following 4 months implantation showing intima (i) and media (m). Note the focal occurrence of the intimal proliferation.

Age intimal thickness from graft sections follows a definite pattern (Figs. 8-10). At almost all locations, the intimal thickness of the superior wall is greater than that of the inferior wall. This is true particularly in the proximal locations of all three groups where the differences between superior and inferior wall intimal thicknesses are statistically significant ($P < 0.05$). Furthermore, there is a tendency for the intimal thickness along the inferior wall to increase from proximal to distal locations, with the distal thickness being greater than the proximal thickness in all groups ($P < 0.05$). The converse of this, superior wall intimal thickness decreasing from proximal to distal locations, was not seen consistently. These differences by graft location are difficult to explain in terms of graft prepara-

FIGURE 8 Average intimal thickness in the $<90^\circ$ proximal angle group of the superior and inferior walls at each of the proximal, middle, and distal locations along the graft length. Superior wall intimal thickness is significantly greater ($P < 0.05$) than inferior wall intimal thickness at the proximal and distal locations.

FIGURE 9 Average intimal thickness in the $90^\circ$ proximal angle group of the superior and inferior walls at each of the proximal, middle, and distal locations along the graft length. Superior wall intimal thickness is significantly greater ($P < 0.05$) than the inferior wall intimal thickness at the proximal and middle locations.
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vation, vessel ischemia, arterial pressure, or blood hormone and metabolite levels alone. Instead they imply the presence of additional factors which themselves vary with graft location.

Wall shear rate is such a factor, and the present data, which portray a weak inverse correlation between it and intimal proliferation, suggest that a relationship exists between wall histopathology and the hemodynamic forces acting within the graft. Fry has shown that fluid forces have a direct effect on the endothelium of dog aortas, defining a critical shear stress (approximately 400 dynes/cm²) below which cells are elastically stretched but above which cells are continually deformed and eventually eroded away. Other studies have considered the shear dependence of macromolecule transport between blood and the vessel wall. Caro et al. initially observed the distribution of fatty streaks and early plaques in the arterial tree of man and theorized that it was coincident with regions of relatively low shear. These regions of early atheroma include the outer walls of Y junctions which Friedman et al. have shown experience low shearing forces similar to those along the superior walls of the vein grafts in this study. A model proposed by Caro et al. hypothesized a cholesterol efflux from the arterial wall to blood, controlled by the concentration gradient of blood cholesterol near the wall. Since a high shear would increase this gradient, and vice-versa, early atheroma would be predicted where shear rates, and thus, concentration gradients, were low. This theory was later modified by Caro and Neren after experiments on the uptake of labeled cholesterol. They too found shear-dependent transport, but concluded that the effect is one of wall shear stress and is on the transendothelial uptake process. Further experiments have shown a direct dependence of labeled albumin uptake upon shear stress where transport appears to be controlled at the fluid-wall interface. A more complex mechanism of transport control has been suggested by Markle and Hollis who found a relationship between shear stress, wall histamine synthesis, and transmural protein uptake in the thoracic aorta. Their results would indicate that histamine synthesis mediates a bio-

chemical mechanism which couples the applied hemodynamic shear stress with the resultant change in arterial wall permeability. Other research has shown reduced gaseous transport and increased platelet deposition in regions of low wall shear. Thus, through its effect on transport between the blood and the vessel wall, fluid shear rates may play a considerable role in the initiation and progression of intimal proliferation. It is also reasonable to assume that regions of low shear rate are more susceptible to thrombus formation and early occlusion due to increased platelet deposition.

Although no other studies to date have addressed the relationship between the fluid wall shear rate and wall hyperplasia as such, several experiments in which histological examination of autologous arterial vein grafts was made do report gross findings. Faulkner et al. using direct replacements of the iliac arteries with autologous veins, found that grafts with a low flow rate (mean, 37 ml/min) had consistently greater intimal thickness over a longer distance than control grafts (mean flow rate, 83 ml/min), whereas grafts with high flow rates (mean, 791 ml/min) had no visible intimal plaques. This is clear evidence that regions exposed to low flow rates and thus, presumably, low wall shear rates, have a greater likelihood for

![Figure 11](image1.png)
hyperplasia. Both Breyer et al. and Bond et al. have specifically studied the degree of subendothelial proliferation in arterial grafts imposed at acute, perpendicular, and obtuse angles to the proximal artery. Breyer et al. found no distinction between groups of varying proximal angles based on the degree of intimal proliferation. Bond et al. concluded that there is a greater intimal proliferation in the proximal end of the acute angle grafts, whereas all other locations in the three groups do not differ significantly. These results generally concur with those of the present study in that there appears to be no sharp distinction in degree of intimal proliferation between angle groups. However, both of these studies consider only whole regions of the graft and do not examine individual wall sections that may be exposed to widely differing shear rates. By measuring the total intimal proliferation in a given graft location, the opposing effects of high and low shear may be combined and offset to produce generally equivalent levels of hyperplasia at corresponding locations of each angle group. The exception cited by Bond et al. of higher proliferation in the proximal region of the acute angle group may be due to the technique used in which only the largest hyperplastic focal regions were measured (personal communication) or to low flow rate conditions in that group.

The results of several clinical studies also may be accounted for by the tendency for intimal proliferation in regions of low shear rate. In particular, Campeau et al., comparing two series of surgical patients, have found that by modifying their bypass procedure, a higher patency rate was achieved. With improved techniques and increased surgical skill, the cumulative patency rate over 1 year rose from 66.8% to 85.4%. Additionally, for all grafts having a flow rate of 50 ml/min, regardless of procedure used, the patency rate was approximately 90%. Those grafts in the modified series with flow 50 ml/min displayed the highest patency rate, 94.7%.

The results of this study establish that the flow is highly asymmetric and time varying within veins grafted in side-to-end anastomoses, and suggest that greater intimal proliferation occurs at sites exposed to low shear rates. Although the exact nature of this fluid-wall interaction is not known, elimination of low shear rate regions, primarily by maintaining high graft flow rates, should reduce intimal growth. Improved graft flow might be achieved through bypass of only critically stenosed vessels and especially those having a good distal run-off, using small caliber grafts to maintain high velocities and possibly even occluding bypassed vessels in order to obtain the maximum graft flow. Additional efforts are necessary, however, to specify the exact mechanisms involved in intimal proliferation and to determine whether other factors are combined with local shear rates to produce this effect.

References

Mechanism of Impaired Water Excretion in Acute Right Ventricular Failure in Conscious Dogs

MEIR YARON AND CLEAVES M. BENNETT

SUMMARY Considerable controversy exists as to what extent left atrial receptors play a role in the physiological regulation of antidiuretic hormone (ADH) secretion. We studied conscious dogs during a stable water diuresis induced by continuous infusion of hypotonic saline, in whom acute inflation of a chronically implanted pulmonary artery balloon consistently produced antidiuresis. Following balloon inflation in nine dogs, glomerular filtration rate (GFR) (67 ± 8 to 70 ± 6 ml/min, P < 0.2) and osmolar clearance (C(Osm)) (3.1 ± 0.2 to 3.3 ± 0.2 ml/min, P > 0.2) did not change. Despite a fall in plasma osmolality (287 ± 6 to 281 ± 5 mOsm/kg H2O, P < 0.02) and rise in mean systemic arterial pressure (100 ± 3.6 to 110 ± 3.8 mm Hg, P < 0.01), urine osmolality rose markedly (88 ± 8 to 187-205, 1973) and renal free water clearance (C(FW)) (7.1 ± 0.8 to 2.9 ± 0.7 ml/min, P < 0.01) both fell. This acute decrease in water excretion was a consequence of a rise in plasma levels of ADH (0.72 ± 0.07 to 2.06 ± 0.20 μU/ml) which returned toward control levels following balloon deflation (1.14 ± 0.18 μU/ml). The changes in ADH levels were shown to be associated with reciprocal changes in left atrial pressure (10.7 ± 1.7 to 6.1 ± 1.5 mm Hg after balloon inflation, returning to 12.2 ± 1.8 mm Hg after deflation). We conclude that in conscious dogs the effects of a small fall in left atrial pressure can predominate over the combined effects of a rise in systemic arterial pressure, continued infusion of hypertonic saline, and a fall in plasma osmolality, to produce a rise in plasma levels of ADH and antiurides.

CHANGES in urine flow rate have been observed following experimental maneuvers and in clinical situations in which left atrial pressure is altered. Henry and Gauer originally proposed 20 years ago that the increases in
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