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EVALUATION OF BLOOD FLOW IN VASCULAR ACCESS GRAFTS
USING THE DOPPLER ULTRASONIC FLOW DETECTOR

by

Marcia Lynne Keen

THESIS

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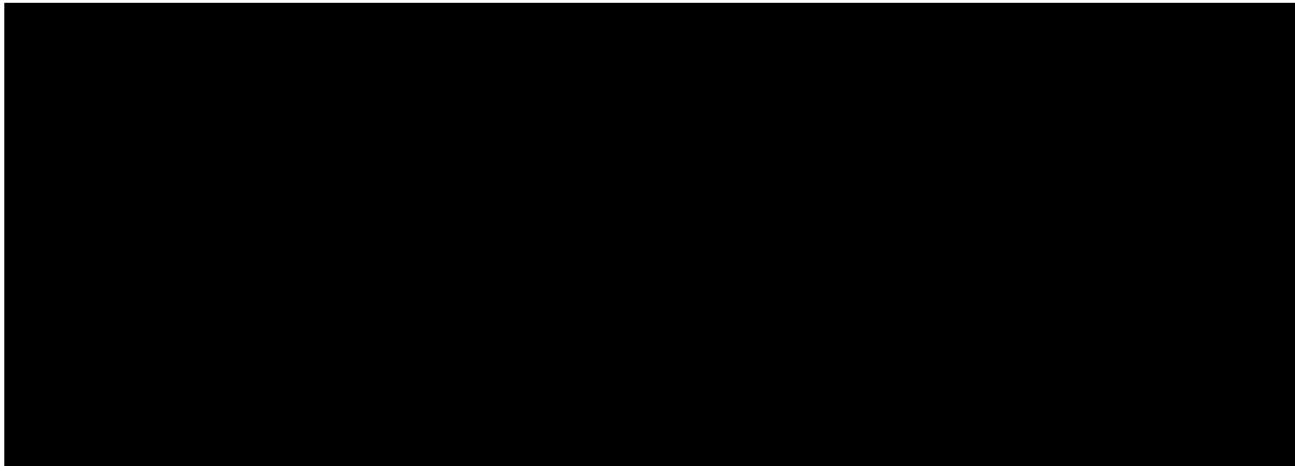
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CHAPTER 1

Introduction to Problem Area

Chronic maintenance hemodialysis now support approximately 70,000 patients in the United States. Federal funding of treatment costs since 1973 and improved technology have produced increasing numbers of long term patient survivors as well as an increased incidence of patients greater than 50 years of age and patients reaching end stage renal disease because of diabetic nephropathy. Successful long term hemodialysis requires adequate vascular access conduits to accomplish therapeutic objectives. Because of a number of physical limitations, many patients require the insertion of heterologous vascular access grafts for suitable access. The two most commonly used grafts are the bovine heterograft and polytetraflouroethylene (PTFE) grafts.

Two physiologic problems may result from the insertion of these grafts. The most common problem is the maintenance of adequacy and/or patency. Thrombosis of the graft may occur and is frequently the result of venous outflow stenosis (Sabanayagam, 1980). Venout outflow stenosis causes a reduction in graft flow and at some critical point, thrombosis occurs.

The second problem that may be seen in patients with arteriovenous fistulas is high output cardiac failure which is secondary to high blood flow through the fistula. Krupski, Bruks, Webb and Effeney (1985) indicate that when fistula flow exceeds 20% of cardiac output, signs and symptoms of intractable cardiac failure may occur in hemodialysis patients.

The daily management of the stable chronic hemodialysis patient and the dialytic therapy is part of the renal nurse's responsibility. Included in this responsibility is the routine assessment of the patient's access to (1) determine patency and suitability for continued use and (2) note any changes in appearance. As such, the routine assessment is restricted to visual examination for signs of infection or complications from previous cannulations and palpation of thrill indicating patency. Patients are instructed to examine their access daily, avoid any prolonged constriction of the graft and to report any unusual symptoms related to it such as tenderness, redness, pain or absence of thrill.

Despite this general assessment by both patient and nurse, the initial sign of access deterioration is most often complete cessation of flow through the graft due to thrombosis. The patient presents for treatment with a non-functioning graft that requires surgical intervention before the patient can be dialyzed. Most often, the thrombosis is due to venous stenosis at or just beyond the graft-vein anastamosis and requires either patch angioplasty or a bypass. If these techniques are not successful, a new graft must be placed and temporary access must be obtained either by subclavian or femoral catheters. These temporary accesses may be painful for the patient and, because of obstruction or infection, may require re-insertion to successfully perform dialysis. Temporary access catheters are utilized for dialysis until the new graft is ready for cannulation, usually 10-14 days, and most patients must remain hospitalized during this period.

The hemodynamic effects of arteriovenous fistulas have been reported

and their contribution to the development of cardiomegaly and congestive heart failure have been recognized (Anderson et al, 1976). Congestive heart failure is a morbid event which is manifested by fatigue, shortness of breath, dyspnea or exertion, and signs of pump failure. Despite careful control of fluid and sodium intake as well as agressive fluid removal during dialysis, the signs and symptoms persist. If it is determined that a high flow fistula is responsible for this persistent clinical picture, surgical reduction of the arterial anastamosis may be required before clinical improvement will occur.

The routine assessment of the vascular access graft does not provide quantitative information about either subtle reductions in blood flow through the graft, reflective of a stenotic venous outflow tract, or excessive flow through the graft which may be responsible for cardiac failure in some patients. At present, measurement of actual blood flow rate through a graft requires invasive radiologic or isotopic examination.

The qualitative access assessment technique currently used by the dialysis nurse is not satisfactory in identifying those grafts in which flow is inadequate or decreasing as a result of venous stenosis, or those grafts in which flow is excessive and subjecting the patient to the risk of high output cardiac failure. Patients continue to require hospitalization and emergency surgical access procedures because of the inability to accurately and simply measure graft flow which is an essential parameter of dialysis therapy. If reliable data on graft flow could be obtained using a non-invasive technique such as the Doppler ultrasonic flow detector, comparison of periodic measurements would provide valuable information for the early detection of changes in the adequacy of graft flow or the

development of high flow grafts by documenting changes in graft flow over time.

Doppler ultrasonic technology is a non-invasive method that has been used to assess blood flow velocity in both arteries and veins (Kreitzer and Lichti, 1975). To calculate volumetric flow from linear velocity measurements, the cross-sectional area (CSA) of the vessel must be known as well as the angle between the incident sound beam and the vessel. This is not feasible in the vascular access grafts used in hemodialysis patients without the use of an invasive procedure. It was postulated for this study that the unique situation provided by the dialysis procedure might allow the quantification of flow rate through the graft in the absence of a known CSA of the graft.

Research Question

Therefore, this study addressed the question: What is the relationship between mean Doppler voltage and blood flow rate through heterologous vascular access grafts measured during dialysis?

Purpose

The purpose of this study was to develop a suitable non-invasive quantitative technique, using available Doppler technology, to quantitate blood flow rate through heterologous vascular access grafts of chronic hemodialysis patients.

Significance of Study

Verification of the linearity of flow rate to mean Doppler voltage would allow the development of a non-invasive in vivo method for vascular

access assessment. To calculate total volumetric flow from Doppler evaluation of flow velocity, the CSA of the graft studied must be known. This is not possible in heterologous grafts since, although the CSA of the graft is known at the time of surgical placement, tissue ingrowth and pseudointimal proliferation may alter the original CSA and therfore alter flow velocity. If the relationship between flow rate and Doppler voltage is linear under the conditions of dialysis, this would allow estimation of flow rate through the graft without knowledge of the graft CSA using the method described in this report.

Validation of the proposed Doppler technique would allow the use of this method by the nurse to quantitatively assess graft flow in hemodialysis patients to determine both adequacy for dialysis and to monitor the graft for the onset of decreased flow, which might signal impending graft failure. Persistent diminution of flow with these measurements would alert the nurse to initiate action to avoid abrupt, unexpected thrombosis of the graft. Utilization of this method could result in timely elective surgical intervention before complete thrombosis occurred. Consequently, the need for temporary access procedures and costly hospitalizations in these patients might be reduced.

The second problem that might benefit from this nursing assessment is the identification of high flow grafts which may impose an excessive burden on already compromised cardiac function that may lead to the clinical syndrome of high output cardiac failure (Anderson et al, 1976). Some reports indicate that high output failure probably occurs only when 20-50% of cardiac output is shunted through a fistula (Anderson et al, 1976; Anderson and Groce, 1975) while others report high output failure

with fistula flows in excess of 1500 ml/min (Ilstrup, Collins, Hanson, and Keshaviah, 1984).

Blood flow rates through the extracorporeal circuit have typically ranged from 200-300 ml/min to achieve adequate solute removal. Recent reports of high efficiency dialysis utilizing blood flows of 400-500 ml/min have generated interest in increasing extracorporeal blood flow rates to reduce treatment time, improve patient response to treatment, and reduce cost (von Albertini, Miller, Gardner and Shinaberger, 1984). Consistent achievement of these flow rates clinically will require adequate fistula flows to successfully implement this therapy. Thus, a third benefit of this technique would be to be able to quantitatively assess vascular access graft flow to insure that adequate flow was available for this approach before attempting to implement this therapy.

Assumptions

1. The heterologous vascular access grafts are inert conduits with vasoactive segments anastamosed at each end of the graft. Therefore, there is no autonomic control or influence on intragraft cross-sectional area.

2. The cross-sectional area of the central body of the graft does not change when some fraction of graft blood flow is diverted through the extracorporeal circuit during dialysis.

Definition of Terms

1. Hemodialysis patient: An end stage renal disease patient receiving chronic maintenance hemodialysis treatments at least twice a week and who has a bovine or PTFE vascular access graft which has

been used for dialysis for at least 3 months.

2. Hemodialysis treatment or procedure: The repetitive process during which a patient's blood is withdrawn, mechanically pumped through a dialyzer for the purpose of water and solute removal and/or addition using the processes of diffusion and convection, and then returned to the patient. This is a procedure used for patients with end stage renal disease for whom the remaining kidney function is inadequate to sustain biological life.

3. Heterologous vascular access grafts: Bovine heterografts or expanded polytetraflouroethylene (PTFE) vascular access grafts placed in a hemodialysis patient's forearm for the purpose of repetitive cannulation for hemodialysis treatment.

4. Central body of the graft (CBG): That section of the graft that, during dialysis, lies between the arterial fistula needle and the venous fistula needle.

5. Mean Doppler voltage (DV): The signal from the mean output mode of the Doppler 806A (Parks Electronics, Beaverton, OR) as recorded on the R1-5D.C.P. strip chart recorder (Parks Electronics, Beaverton, OR) and expressed as volts.

6. Doppler probe: The 15° angle flat probe with a nominal 9.3 mHz frequency (Parks Electronics, Beaverton, OR).

7. Flow velocity: The flow rate of milk through a simulated access graft of known cross-sectional area passing the site of Doppler probe placement and expressed as cm/sec.

8. Extracorporeal or dialyzer circuit: This circuit consists of the arterial and venous fistula needles, the arterial and venous blood

lines, the blood pump segment and the dialyzer which forms a parallel circuit to the central body of the graft during the dialysis procedure.

9. QB: The blood flow rate through the extracorporeal circuit during dialysis, expressed as ml/min.

10. Qmilk: The flow rate of milk through the in vitro system, expressed as ml/min.

11. Qg: The in vivo total graft flow rate through a vascular access graft calculated from linear regression analysis of Doppler voltage on QB or calculated from pertechnetate infusion studies, expressed as ml/min.

Limitations

1. This study used a convenience sample and the actual number of different vascular access grafts studied is small.

2. In the majority of the patients, small internal diameter PTFE grafts (5 mm) were placed by the same access surgeon. This may account for the large number of lower graft flows found in this population.

3. To employ this Doppler technique to measure graft flows, both fistula needles must be placed in the single main channel for blood flow through the graft. This would seem to exclude the use of this technique with endogenous arteriovenous fistulas in which any runoff channel exists between the two cannulation sites.

4. The 15° angle flat probe does not provide the optimum angle for the Doppler technique. This shallow angle dictates that the Doppler beam travel a greater distance before intersecting the blood vessel and therefore the signal is attenuated. Therefore, the use of this probe may have to be restricted to superficial access grafts.

5. All grafts studied were placed in the forearm to facilitate probe placement. No upper arm or leg grafts were studied.

CHAPTER 2

Literature Review

Vascular Access Grafts

Surgically created arteriovenous fistulas are the access of choice for long term hemodialysis therapy (Brescia, Cimino and Appel, 1966). Because of a number of recognized physical constraints associated with the aging or diabetic patient as well as iatrogenic loss of suitable blood vessels that may occur with long term survival on hemodialysis, this mode of dialysis access is not feasible for a number of patients (Wilson, 1982). Consequently, many patients must have heterologous vascular grafts placed as the primary or secondary access mode. The two most common materials now in use for heterolgous grafts are bovine heterografts and expanded polytetraflouroethylene (PTFE) grafts.

Bovine heterografts are bovine carotid arteries which are subjected to an enzyme tanning process. They range from 7.5 to 9 mm in diamter and have been used successfully in the creation of an access graft suitable for dialysis patients (Kaplan et al, 1976). They are used less frequently now since the introduction of PTFE which provides some advantages in cost, available sizes, ease of placement, histologic processes after placement, and resistance to intragraft infection (Baker, Johnson, and Goldfarb, 1976).

Expanded PTFE is a synthetic graft which, upon maturation, develops a neointima throughout the intragraft surface. Neocapillary formation and tissue ingrowth into the graft walls help to nourish the neointima and, with time, this is felt to become living tissue. The amount of

tissue ingrowth cannot be controlled and may become excessive and limit flow through the graft. These grafts can be manufactured with variable internal diameters (4-10 mm) to accommodate variable anastamotic requirements. The neointima requires time to progress to the point where satisfactory homeostasis can be achieved after cannulation. This period of time is variable but is considered to be at least 7 days (Baker et al, 1976).

Both bovine and PTFE grafts are subject to complications such as thrombosis, infection and pseudoaneurysms, with thrombosis being the most common complication (Rapaport, Noon and McCollum, 1981; Lilly, Nghiem, Mendez-Picon, and Leen, 1980). Late failure of the graft from thrombosis is most often due to venous stenosis at or just beyond the graft-vein anastamosis. Examination reveals a pearly white excresence of collagen which occurs circumferentially beneath the endothelium of the arterialized vein usually starting a few millimeters to 2 cm distal to the anastamosis. There is some evidence that this subendothelial hyperplasia is associated with shear stress and turbulence of a jet stream of blood entering the vein at high velocity (Dienst, Oh, Levin and Kallioinen, 1983). The incidence of this complication in heterologous grafts is variable and rates ranging from 15-89% at 3 years are reported (Rapaport et al, 1981; Silcott, Vannix and DePalma, 1980). There is no consensus about the greater susceptibility of one material compared to the other (Doyle and Fry, 1982; Salmon, 1981).

Venous stenosis requires time to develop and as outlet resistance rises, flow through the body of the graft decreases. Several authors (Viera and Arango, 1979; Rosenthal, 1982; Doyle and Fry, 1982) identify

increased venous resistance, as measured in the extracorporeal circuit,
as a sign of a stenotic lesion justifying radiographic examination for
verification. Venous resistance, as measured in the outflow portion of
the extracorporeal circuit, is influenced by needle size and placement
in the graft and therefore may mask the pressure effects of a developing
stenosis. Jenkins, Buist, and Glover (1980) reported that in 16 of
40 PTFE grafts, thrombosis was the first indication of a stenotic lesion.
Therefore, this complication can develop undetected. The significance
of this problem can be seen in the multicenter study reported by Aman,
Levin, and Smith (1980). The study population consisted of 465 dialysis
patients where it was shown that thrombosis of vascular access was the
most frequent reason for hospital admission in these patients (55.2%).

Venous stenosis leading to reduced flow through the graft can compromise
dialytic therapy by producing recirculation of dialyzed blood into the
extracorporeal circuit (Gotch, 1976). Pump-assisted blood flows for
dialysis are usually 200-300 ml/min to accomplish therapy objectives with
respect to solute removal. The efficiency of this process relies on
fresh systemic blood entering the circuit. If graft flow is less than
the amount required by the pump, dialyzed blood returning to the venous
end of the graft will be drawn back into the arterial needle. This
admixture of venous and systemic blood is at a lower concentration;
therefore, total solute removal during dialysis will be reduced and end
dialysis blood concentrations will be above desired levels. Continuation
of this process may culminate in the patient being inadequately dialyzed
with the consequence of the possible development of uremic complications
such as pericarditis, gastritis and metabolic acidosis (Parker, Laird,

and Lowrie, 1983). Therefore, even short of thrombosis, undetected reduced access blood flow has serious consequences (Gotch et al, 1976).

In summary, heterologous vascular access grafts are used as primary or secondary vascular access in hemodialysis patients. Unfortunately, they are subject to a number of complications, including thrombosis secondary to venous outflow stenosis. The signs of this developing lesion may be so subtle as to escape detection with routine monitoring. Therefore, cessation of flow and thrombosis may occur unexpectedly with serious consequences for the patient.

Hemodynamic Effects of Fistulas

Vascular access grafts are surgically placed between an artery and vein and in the forearm can be inserted in either a loop or straight configuration as shown in Figure 1. This then produces a circulatory anomaly which results in a decrease in total peripheral resistance and a compensatory increase in cardiac output. Cardiac output is primarily determined by venous return. The marked decrease in total peripheral resistance resulting from a large arteriovenous fistula (often additive to a similar effect of anemia in these patients) results in high venous return rate and consequent increase in cardiac output. If the ventricular function curve is normal, increased cardiac output results without substantial increase in ventricular filling pressures and manifestations of heart failure. If there is a myocardial abnormality (common in end stage renal disease patients) and/or the fistula is very large, the cardiac output and venous return curves will intersect at high right atrial filling pressures and variable increase in cardiac output resulting in clinical manifestations of heart failure despite increased cardiac output.
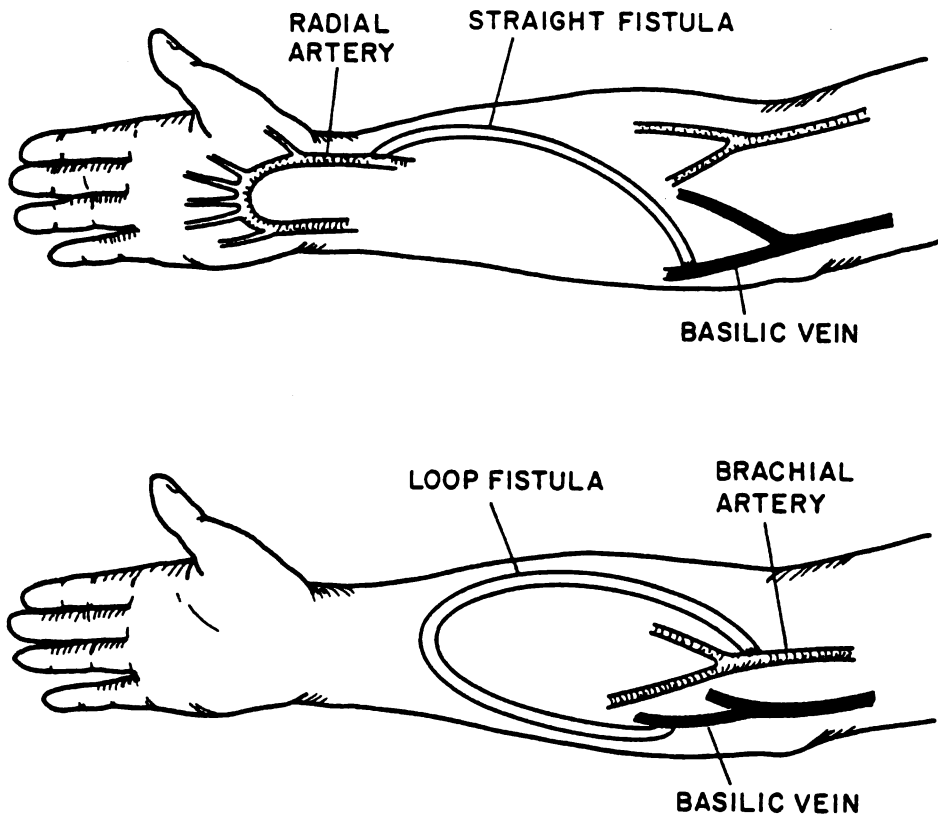
Straight fistula and loop fistula.

FIGURE 1

Cardiomegaly, systolic bruits, gallop rhythm and an abnormal EKG may

be present in the asymptomatic patient with an arteriovenous fistula

(Braunwald, 1980).

Patients with chronic renal failure are frequently hypertensive,

usually anemic, and may be significantly hypervolemic because of dietary

salt and fluid indiscretions. Thus, the contribution of arteriovenous

fistulae in the development of cardiac failure may be modest. However,

reports in the literature suggest that, in a small number of patients,

excessive flow through the fistula may produce intractable cardiac failure

which resolves when flow through the fistula is reduced.

Anderson and colleagues (1976) reported data on 15 patients with

high output cardiac failure related to forearm arteriovenous fistulas.

Data on 9 patients was based on a review of the available literature.

The remaining 6 patients were new cases presented by the authors. A

decrease in heart rate after fistula occlusion for 5 minutes (Nicaladoni-

Branham sign) was reported in only 4 of the patients. Fistula flows

in 6 of these patients, as measured with an electromagnetic flow meter

(EFM) at the time of surgery, ranged from 0.6 to 2.9 liters/min with a

mean flow rate of 1.5 liters/min. Decreases in cardiac output with

temporary fistula occlusion, measured in 5 of the 15 patients, ranged from

0.3 to 11 liters/min with an average of 2.9 liters. Surgical banding of

the fistulas to reduce flow produced resolution of symptoms and physical

findings of heart failure in 13 of 15 patients. These authors felt that

the incidence of this cardiac complication in patients with arteriovenous

fistulas was small as indicated by the small number of patients reported

in the literature at the time of this review. However, certain patients

with intrisinc cardiac disease may be susceptible because of the increased

cardiac output resulting from the fistula.

In 1978, von Bibra, Castro, Autenrieth, and Gurland evaluated the

effects of arteriovenous fistulas on cardiac function in 7 dialysis patients

using echocardiography. Four of the patients had external Scribner shunts

and the remaining 3 patients had PTFE grafts in place. Parameters of

cardiac function were measured with the fistula or shunt open and after

10 minutes of fistula or shunt occlusion. With the access occluded,

heart rate, cardiac output and cardiac index fell significantly ($p < 0.005$).

Blood pressure and stroke volume did not change, nor did ejection fraction.

As a group, measures of cardiac contractility did not change. The authors

felt that those patients with left ventricular hypertrophy and thus prone

to reduced compliance may benefit from smaller fistula flow rates for

optimal cardiac performance. The inclusion of 4 patients with acute

renal failure and external shunts makes the generalizability of these

results difficult. These patients did not have long exposure to pressure

and volume overloading that is more common in chronic hemodialysis

patients. Also, M-mode echocardiography does not actually measure left

ventricular volume. If the left ventricle is segmentally diseased, the

change in left ventricle diameter as measured by this method may be

erroneous.

O'Regan, Lemaitre and Kaye (1978) measured sequentially PTFE graft

flow and cardiac output in 21 hemodialysis patients using infusion and

indicator dilution methods respectively. Mean blood flow rates through

PTFE grafts varied from 0.276 to 3.84 liters/min with a mean flow of

1.9 liters/min. Mean cardiac output in these patients was 7.1 liters/min

with a cardiac index of 4.0 liters/min/m^2. Blood flow through the graft

did not correlate with systolic or diastolic blood pressure. However,

a significant correlation between graft flow and cardiac output and index

was found ($p < 0.001$). Two of 21 patients developed cardiac failure which

was thought to be secondary to large graft flows. The graft flows in

these two patients were 3.8 and 2.3 liters/min. Graft flow was decreased

to 0.8 and 2.1 liters/min respectively through surgical banding of the

arterial anastamosis. Following this procedure, resolution of cardiac

failure was achieved. The authors felt that the incidence of this

complication was small (2/21) but that increased graft flow may be a

critical factor in the development of cardiac failure when cardiac

reserve is already compromised by other factors. Graft flow measurements

in these 21 patients identified 2 grafts with venous outflow stenosis

and the authors felt that this permitted simple surgical intervention

which was successful in salvaging these grafts. The methods described

in this study are invasive and must be done when the patient is not on

dialysis. The sample population included some patients who had not

initiated dialysis therapy.

VanderWerf, Kumar, Pennel, and Gotlieb (1978) reported 3 patients with

high flow bovine grafts. All patients had refractory cardiac failure

which did not improve with standard clinical management. Actual graft

flow was measured using the pertechnetate infusion method described by

Gotlieb, Garcia, and Cold (1976) before and after surgical reduction of

graft flow. Preoperative graft flows were 2.8, 2.85 and 3.3 liters/min

which were reduced to 0.80, 0.75, and 0.70 liters/min respectively.

Cardiac output in these patients was measured using the thermodilution

technique pre and postoperatively. No significant change in cardiac

output was seen but clinical improvement was seen in all patients after

graft flow reduction.

In summary, the studies of the hemodynamic effects of arteriovenous

fistulas and grafts showed that high output cardiac failure may occur

in the presence of high flow accesses in hemodialysis patients.

Non-invasive assessment of this phenomenon (Branham's sign) provides

inconsistent results. The actual incidence of high output cardiac

failure appears to be small although many of the reports cited above

do not provide population size. Differential diagnosis of cardiac

failure may be difficult until fistula flow is surgically reduced and

clinical improvement occurs.

Invasive Measurement of Vascular Access Graft Flow

Several invasive methods have been reported that can be used to

measure total graft flow. Gotlieb et al (1976) described an infusion

method using pertechnetate, a technecium-labeled compound, to quantitatively

measure bovine graft flow in 17 hemodialysis patients. At the time of

surgical placement of the graft, a constant infusion of isotope was given

in the afferent limb of the graft and samples were obtained from the

efferent limb and counted for isotope. The count rate of each efferent

sample was plotted semi-logarithmically against time and the best fit

line extrapolated back to zero. Graft flow was calculated using the

relationship

$$\text{Graft blood flow rate, ml/min} = \frac{(\text{Infusate counts/min})(\text{Infusion rate, ml/min})}{\text{Efferent counts/min}}$$

The graft flow was also measured using an electromagnetic flow meter intraoperatively just prior to the infusion study.

The two methods agreed very well with an r value of 0.962 (p<0.01). No complications from the procedure were observed and the small amount of isotope infused (less than 100 microcuries) made it a safe procedure. It did, however, represent an invasive procedure.

Kaye, Lemaitre and O'Regan (1977) used a modification of this method in 15 patients with PTFE grafts. Samples for radioactive counting were obtained from both afferent and efferent limbs of the graft with the isotope infusion site located between these two sites (see Figure 2). Graft flow was then calculated using the following expression:

$$\text{Graft flow rate, ml/min} = \frac{\text{Counts infused/min}}{\text{Venous counts/ml} - \text{Arterial counts/ml}}$$

Graft flow was measured at the same time using a Doppler ultrasonic flow detector in 7/10 patients. The comparison of graft flows obtained with these two methods yielded an r value of 0.81 (p<0.01). The infusion method was used to re-evaluate graft flow in 8 patients and was found not to differ significantly from the previously measured graft flow. No complications were observed following the isotope measurements. No information was given about how volumetric flow was calculated from the Doppler measurement of velocity, and no standard deviation was given for the isotope measurements to indicate the variability encountered.

The pertechnetate infusion method as described in these two studies has been developed for use in the measurement of total fistula flow rate. The method has been validated through the use of the electromagnetic flow meter in one study and with a single point Doppler study in the
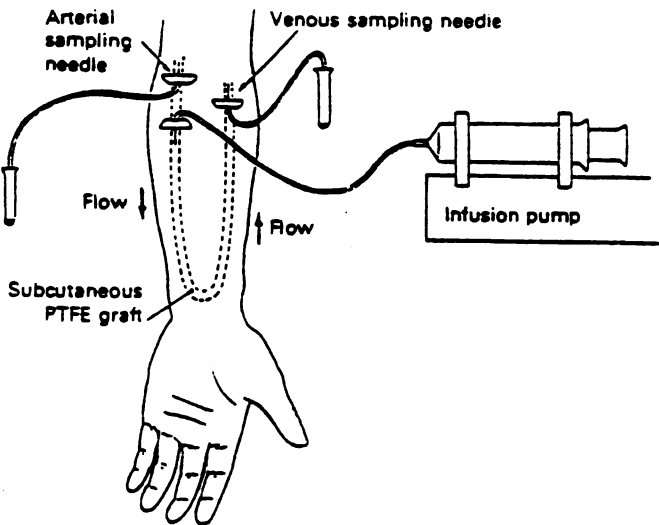
FIGURE 2

other. This infusion method is rapid, easy to perform and appears to
carry minimal risk to the patient since the amount of isotope infused
is small. It is, however, an invasive procedure.

The Doppler Studies

The Doppler effect, first described in the mid nineteenth century,
describes the characteristics of the sound frequency of a moving particle,
with a higher frequency emitted from a particle moving towards the listener
and a lower frequency emitted from a particle moving away from the
listener. This change in frequency, as a result of interface with moving
objects such as erythrocytes, is known as the Doppler shift (Forsberg, 1980).

The principle of the Doppler ultrasonic flow detector is based on
this phenomenon and is shown in Figure 3. Oscillating current is applied
to a piezoelectric crystal which produces a beam of continuous wave
ultrasound of a known frequency which can be directed transcutaneously
toward a blood vessel. As the sound frequency intercepts erythrocytes
moving toward the crystal, the reflected frequency, picked up by a
second piezoelectric crystal, is higher in frequency. If the erythrocyte
is moving away from the probe, the receiving crystal will pick up a
lower frequency. This shift in frequency is proportional to the velocity
of the moving erythrocyte. The shifted frequencies produced by motion
are compared to the emitted frequency. This frequency difference is
converted to proportioate voltage. Zero-crossing circuitry in the
bi-directional Doppler equipment is used to determine the average
frequency shift and to convert it to a proportional electrical signal
which can then be recorded on a strip chart recorder (Shoor, Fronek
and Bernstein, 1979).
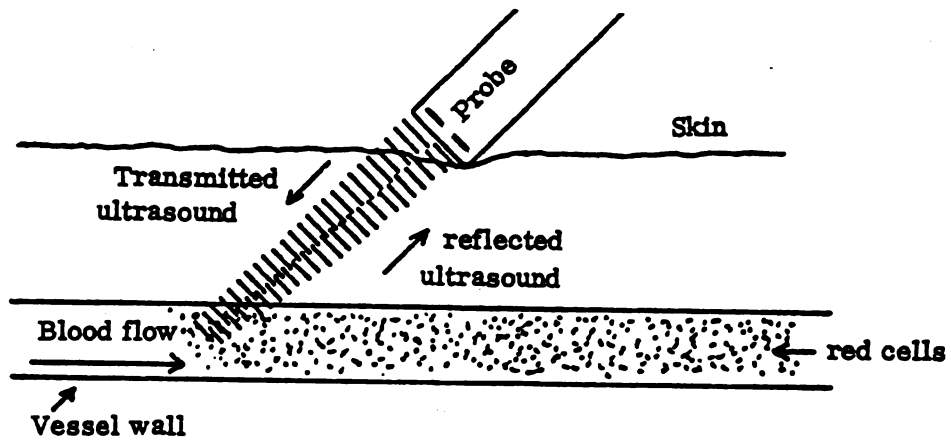
DOPPLER ULTRASONIC FLOW DETECTOR

FIGURE 3

The Doppler equation for mean velocity ($\overline{V}$), cm/sec is:

$$\overline{V} = \frac{C\overline{\Delta f}}{2fe(\cos\theta)}$$

where C = velocity of the sound in the medium being studied which, in the case of blood, is $1.56(10^5)$ cm/sec; $\overline{\Delta f}$ = mean frequency shift; fe = emitted frequency; θ = angle of the incident sound beam with the object path.

Knowing the mean velocity permits calculation of volumetric flow if the internal diameter of the vessel studied is known (LoGerfo et al, 1976). This can be done using the following equation:

$$\text{Cross-sectional area, } cm^2 = \frac{\pi D^2}{4} = \pi r^2$$

Thus, volumetric flow can be calculated using the following expression:

Flow rate, ml/min = 60(Cross-sectional area · Linear velocity)
However, in transcutaneous applications, this is rarely possible. Internal diameter of vascular access grafts is known at the time of surgical placement but itssue ingrowth and pseudointimal proliferation may alter the original diameter and therefore alter the relationship between flow rate and velocity, since flow rate is proportional to the square of the vessel radius.

To summarize, Doppler technology relies on the proportionality of the Doppler frequency shift to the rate at which erythrocytes are moving to determine velocity. The Doppler appears to be an acceptable, non-invasive and simple technique to measure blood flow rate if the cross-sectional area of the vessel under study is known.

Use of the Doppler to Measure Vascular Access Flow

Doppler technology has been used extensively in evaluating vascular blood flow and diagnosis of occlusive vascular disease (Risoe and Wille, 1978; Johnston, Maruzzo and Cobbold, 1978). The obvious advantages of using this technology in such clinical situations is that it is non-invasive, is relatively easy to use, utilizes equipment of moderate cost and is portable. In contrast, angiography carries the risk of intimal damage or hematoma formation (Fogarty and Krippaehne, 1965). Keitzer and Lichti (1975) reported that diagnoses of sites of stenosis and occlusion established by Doppler and radiologic techniques were comparable.

The body of literature addressing the use of standard Doppler equipment to quantitate angioaccess flow in dialysis patients is small. All studies were done on non-dialysis days and most studies report results from surgically created arteriovenous fistulae (AVF). The incidence of failure in AVF due to thrombosis is significantly less than the incidence in heterologous grafts (Aman et al, 1980).

Forsberg (1980) studied 45 patients of varying ages in whom an AVF had been in place for a mean of 6 months. Doppler mean flow velocity in these fistulae was 52 ± 14 cm/sec with a range of 23 to 84 cm/sec. Volumetric flows were calculated based on angiographic estimation of vessel internal diameter. The calculated flows ranged from 157 to 1254 ml/min. There was an inverse correlation between age and flow velocity measured. The author states that adequate function can be defined as 50 cm/sec with a range of 30-70 cm/sec. The ability to calculate volumetric flow from Doppler measurement in this study required an invasive estimation of vessel cross-sectional area.

Forsberg, Tylen, Olin and Lindstedt (1980) reported data in 14 males with AVF comparing quantitative flow obtained using Doppler equipment and volumetric flow calculated from dye-dilution studies done at the same time. The forearm fistulas were examined with brachial angiography. Volumetric flow was calculated from the Doppler evaluation based on the measurement of the brachial artery. The Doppler output was recorded as a velocity profile necessitating calculation of a mean velocity from this wave·form. This mean velocity was then multiplied by the estimated cross-sectional area of the brachial artery to obtain volumetric flow. The dye dilution method was carried out by bolus injection of green dye while venous blood was continually sampled and passed through a spectrophotometer. The two methods correlated well ($r = 0.91$). In this series of male patients, ages unknown, mean flow was 1590 ml/min which was considered very high. The authors conceded that error in over or underestimation in the size of brachial artery by 0.5 mm could produce a 10-20% error in calculated graft flow from the Doppler evaluation. In 1 patient with high output cardiac failure, at the time of surgery to reduce fistula flow, simultaneous measurement of graft flow was done using the Doppler and dye dilution techniques as well as an electromagnetic flow meter. It was puzzling that good agreement was obtained between the Doppler and flow meter techniques (2.9 vs 2.5 liters/min) but the dye dilution technique, which had previously correlated well with the Doppler calculated flow, gave a flow rate of 4.9 liters/min, well above the flows obtained with the other two methods. The authors did not comment on this discrepancy. Both the dye dilution technique and the electromagnetic flow measurements are

invasive methods that carry some risk to the patient.

Forsberg, Holmin and Lindstedt (1980) reported quantitative flow measurement in AVF in 83 patients, only 29 of which were dialysis patients. Time studied after creation of the fistula ranged from 2 months to 10 years in this population. Mean velocity in this group of patients was 45 cm/sec and, using the internal diameter of the feeder brachial artery, measured by B-scan ultrasound, mean volumetric flow was estimated at 634 ml/min. No correlation was found between age of the fistula and volumetric flow. In this group, no correlation was found between flow velocity, volume flow, and diameter of the brachial artery. The authors stated that the Doppler techniuqe combined with B-scan ultrasound evaluation of the brachial artery could be used to recognize changes in fistula flow in individual patients. No other method was used to validate the Doppler technique. There was no information given about the sequence of measurements and it is not known what period of time elapsed between the measurements which might have influenced the calculated values.

These three Swedish studies looked at flow velocities in AVF after variable placement times. No data was reported on the assessment of linearity of Doppler signal to flow velocity in heterologous grafts. Although in vitro calibration of the Doppler preceded each in vivo application, linearity of signal to flow was not reported in these studies in AVF. This was probably due to the inability to manipulate flow rate through these fistulae under known conditions. The dialysis patient population tended to be younger than the U.S. population which probably influenced the predominance of AVF rather than heterologous grafts in these patients. The purpose of all these studies was to examine the range of

fistula velocities in these populations primarily to assure adequate flows but avoid excessive flows which might produce a steal syndrome in the extremity, or high output cardiac failure. Adequate flow velocity was considered to be 50 cm/sec with a range of 30-70 cm/sec. This was defined independent of feeder brachial artery diameter. Two of the 3 studies required an invasive procedure to estimate fistula internal diameter.

Levy, Bourquelot, Ponsin, Man and Martineaud (1984) reported on the results of AVF blood flow measurement in 29 dialysis patients using a new range gated, double transducer Doppler. This apparatus is designed, through the use of the range gated system to determine the internal cross-sectional area of the vessel studied. The double transducer component measures the angle of the incident sound beam and the transected vessel. Thus, volumetric flow can be calculated from these results and a measurement of linear velocity. These measurements of flow were compared to intraoperative measurement of fistula flow using an electromagnetic flow meter. A statistically significant correlation between these two methods was seen with an r value of 0.68 (p<0.001). The mean values for fistula flow with the Doppler was 821 ml/min and with the electromagnetic flow meter was 756 ml/min. The new range gated Doppler equipment is not portable and requires sophisticated wave form analysis. It does not seem amenable to rapid, simple bedside measurements.

Bouthier and colleagues (1983) used the same range gated Doppler system to evaluate fistula blood flow rate in 32 dialysis patients. All measurements were repeated at least twice and mean reproducibility was 5% for velocity and 7% for internal diameter of the vessel. With

radial arteriovenous fistulas, mean blood flow rate was 728 ml/min while brachial fistulas had a mean blood flow rate of 778 ml/min. Seven of 32 patients had bovine heterografts and blood flow averaged 1,225 ml/min. The authors reported less than 2% error in estimating the angle between the ultrasound beam and vessel axis. Validation of this Doppler technique was performed using an in vitro test device.

Fistula flow measurement methods using standard Doppler equipment have been described. Several of these methods rely on an invasive technique to estimate or measure cross-sectional area of the fistula. Cross-sectional area has also been measured using echocardiographic examination of the fistula. If this information can be obtained, volumetric fistula flow is calculated from cross-sectional area and linear velocity.

A range gated, double transducer Doppler has been used to obtain both linear velocity and cross-sectional area non-invasively in fistulas used for hemodialysis. This equipment is complicated, cumbersome and requires sophisticated analysis of wave form recording thereby rendering it unsuitable for use during the dialysis procedure.

Conceptual Framework

Vascular access grafts are commonly employed in patients for dialysis therapy. Because of their semi-rigid structure, flow through the graft is not controlled by intragraft contractility or distensibility, although the influence of systemic blood pressure on the feeder artery has not been documented. These prosthetic grafts do not represent host tissue, and flow characteristics through the access, particularly at

the venous anastamosis, do not match those found in endogenous vasculature. A common problem in these grafts is thrombosis, most often due to venous stenosis. As this lesion develops, flow through the graft decreases over time until the end point of thrombosis is reached. Decreased intraluminal diameter because of the stenotic lesion increases resistance to flow which may slow flow through the graft body. The internal diameter of the graft is known when surgical placement is performed. However, maturation of the graft results in variable tissue ingrowth of the graft body and neointimal proliferation along the intraluminal wall. These anatomical changes in the graft alter the internal diameter and, therefore, measured velocity as a function of constant blood flow.

To use current continuous wave Doppler equipment to measure volumetric graft flow, both the internal diameter of the vessel studied as well as the exact angle of the transcutaneous sound beam to the vessel must be known. This is not possible for in situ grafts for the reasons described earlier. However, an estimate of total volumetric flow rate through these grafts could be obtained by development of a mathematical relationship between volumetric flow rate and Doppler voltage based on several known changes in graft flow rates.

The Doppler studies cited previously examined linear velocity at the prevailing fistula flow rate. Forsberg, Holmin and Lindstedt (1980) estimated internal diameter of the feeder brachial artery from B-scan ultrasound in an attempt to quantitate flow. There were no studies which attempted in vivo calibration of mean Doppler voltage to flow velocity in order to estimate volumetric flow.

The present study proposed using the extracorporeal circuit,

established for the purpose of providing dialysis therapy, to manipulate volumetric flow through the graft and record mean Doppler voltage at the respective flow rates. A mathematical expression would then be developed relating several measurements of blood flow and the respective mean Doppler voltage recordings. This relationship could then be used to calculate total volumetric flow through the graft even though graft internal diameter is unknown.

During hemodialysis, blood flow in the extracorporeal circuit (QB) is regulated and held constant by a roller pump. The actual dialyzer blood flow rate (QB) prescribed is dictated by solute removal to be achieved during treatment and QB usually ranges from 200-300 ml/min (Gotch and Sargent, 1985). The actual volumetric flow through the dialyzer can be precisely measured (Gotch, 1976). Thus, the extracorporeal circuit is, in fact, a parallel circuit to the graft with blood leaving the graft close to the arterial anastamosis and returning to the circulation close to the venous anastamosis. thereby bypassing the central body of the graft (CBG).

Figure 4A shows the flow conditions in the graft when no flow is being diverted through the dialyzer circuit or when QB = 0 ml/min. Therefore, the total blood flow rate through the CBG is equal to that entering the graft at the arterial anastamosis. As shown in Figure 4B, during dialysis, some blood flow is diverted at the arterial end of the graft, pumped through the dialyzer circuit and returned to the patient close to the venous anastamosis, thereby bypassing the CBG. The quantity of blood pumped through the dialyzer, which is then a parallel circuit to the graft, bypasses the CBG. By increasing QB through the parallel

FIGURE 4A

FIGURE 4B

EFFECT OF DIALYZER CIRCUIT FLOW RATE
ON
CENTRAL BODY GRAFT FLOW RATE

Dialyzer

Central
Body of
Graft

QB = 0 ml/min

Dialyzer

Central
Body of
Graft

QB = 300 ml/min
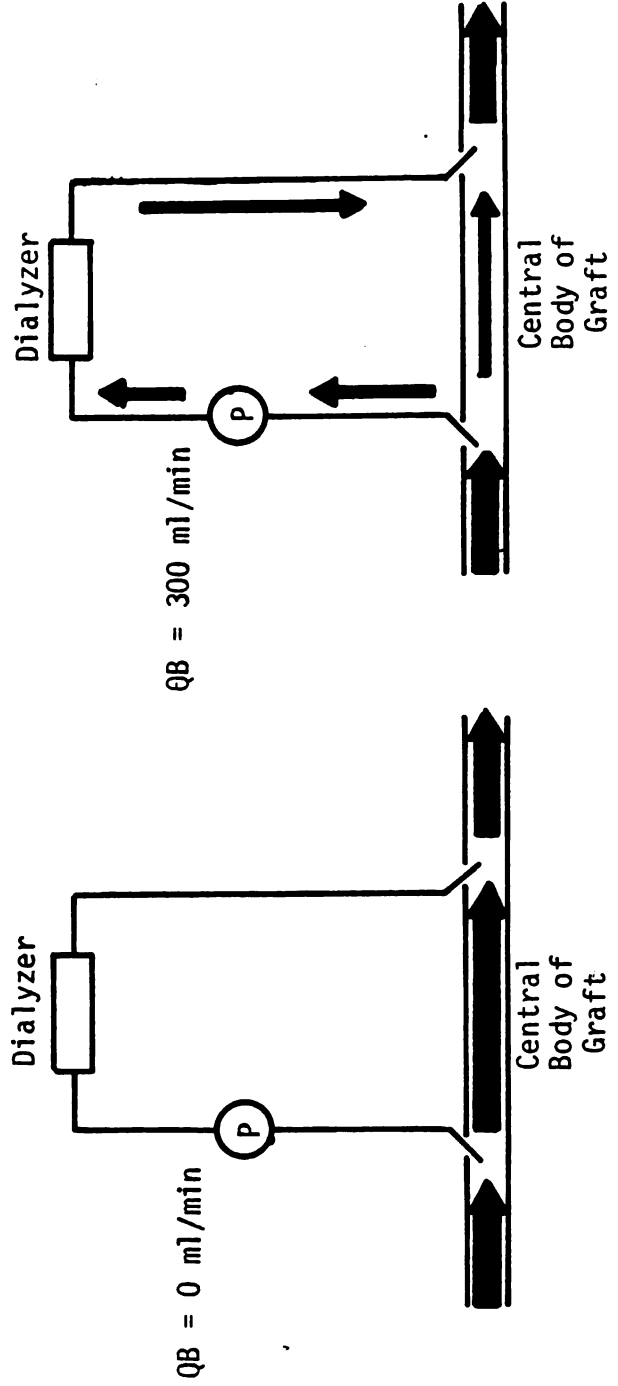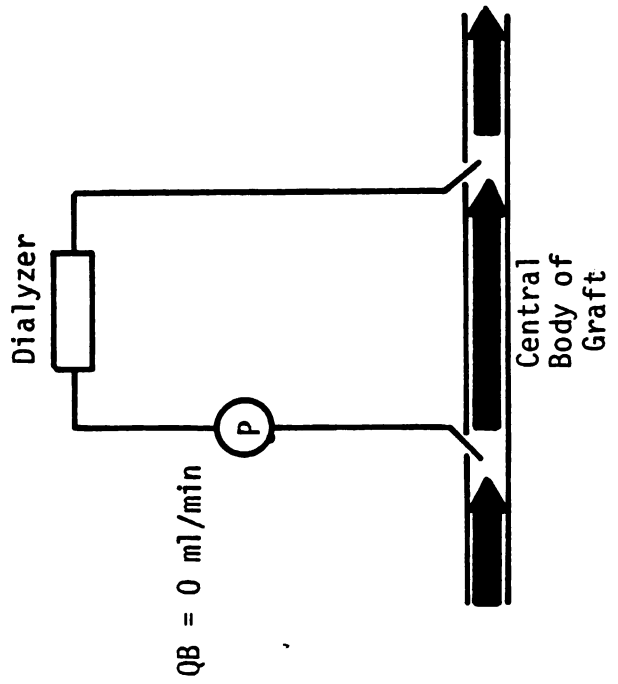
dialyzer circuit, blood flow through the central body of the graft can be reduced by precisely known decrements of flow.

By placement of the Doppler probe over the CBG and measuring Doppler voltage at selected dialyzer circuit flow rates, one could measure variable graft flow rate through the manipulation of QB. As shown in Figure 4A, Doppler voltage could be recorded when the parallel circuit was not operating or when total graft flow (Qg) was moving through the CBG past the probe site. As shown in Figure 4B, as QB is increased and thus Qg through the body of the graft is reduced by the same amount, mean Doppler voltage could also be measured and recorded. Therefore, with Doppler probe placement constant, Doppler voltage could be measured at variable flow rates through the graft.

Figure 5 depicts a set of simulated data to show the relationship of Doppler voltage and several precisely measured dialyzer circuit flow rates. When QB is zero, total graft flow is through the central body of the graft and Doppler voltage is maximal and represented by the ordinate intercept on this figure. As QB is incrementally increased, central body graft flow is decreased by the same amount and, consequently, Doppler voltage decreases as shown on this figure by the data points at QB 100, 200 and 300 ml/min. The Doppler voltage is expected to decrease linearly with volumetric decrements in CBG since linear flow velocity is directly proportional to volumetric flow rate. Therefore, linear regression of these data to the abscissa, at which Doppler voltage is zero, will define the QB which would be required if total graft flow was diverted through the dialyzer circuit and thus totally bypassed the central body of the graft. This extrapolated value is then equal to total graft flow.
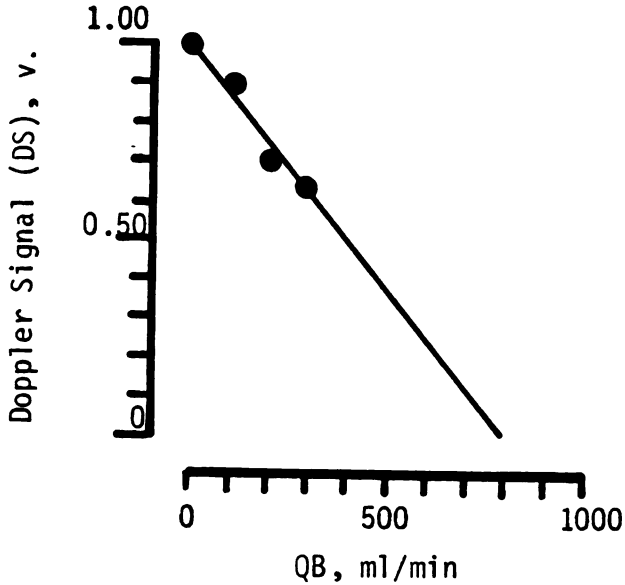
SIMULATED IN VIVO DATA OF
DOPPLER SIGNAL vs QB

FIGURE 5

Summary

Heterologous vascular access grafts inserted in hemodialysis patients are subject to the development of stenotic lesions and in a small number of patients may contribute to high output cardiac failure. The ability to measure graft flow would facilitate the accurate diagnosis of these undesirable clinical conditions. Most methods used to measure graft flow require invasive radiologic or isotopic techniques. In order to use standard Doppler equipment to quantitate graft flow, the vessel internal diameter must be known. This necessitates invasive estimation of this parameter or the use of complex Doppler equipment to elicit this information. The method used for this study proposed using the extracorporeal circuit to vary the blood flow rate through the graft during dialysis and, from these measurements, develop a mathematical relationship to calculate total graft flow in the absence of a known graft internal diameter.

CHAPTER 3

METHODS

This study consisted of 2 phases. Phase 1 was designed to establish in vitro reliability and validity of the Doppler technique for use in vivo. To accomplish this, we established the linearity of the mean Doppler voltage output to flow velocity, and determined the effect of probe angle on the linearity of the voltage velocity relationship. Phase 2 consisted of in vivo application of the proposed Doppler technique to quantitatively assess vascular access graft flow in dialysis patients.

In Vitro Studies

In Vitro Test Circuit

The in vitro system is shown schematically in Figure 6. This system was composed of an 8 liter (L) open glass reservoir, a 2 L stoppered Erlenmeyer glass flask, 1/4 inch internal diameter (ID) Tygon tubing, 1/4 inch ID polyvinylchoride pumping segments, a DWS Model 7401 double header roller pump (B-D Drake Willock, Portland, OR), and a 3/16 inch ID silastic segment with Latex cuff as the Doppler placement site. The dual header pump provided a maximum volumetric flow of 820 ml/min. This dictated the use of the 3/16 inch ID tubing for the Doppler probe placement to produce linear flow velocities up to 80 cm/sec. Flow velocities of up to 80 cm/sec was chosen to cover the range of blood flow velocities expected in vivo with a 6 mm ID PTFE graft. The same headers were used for all studies to avoid the introduction of variability in flow rate due to variations in header ID.
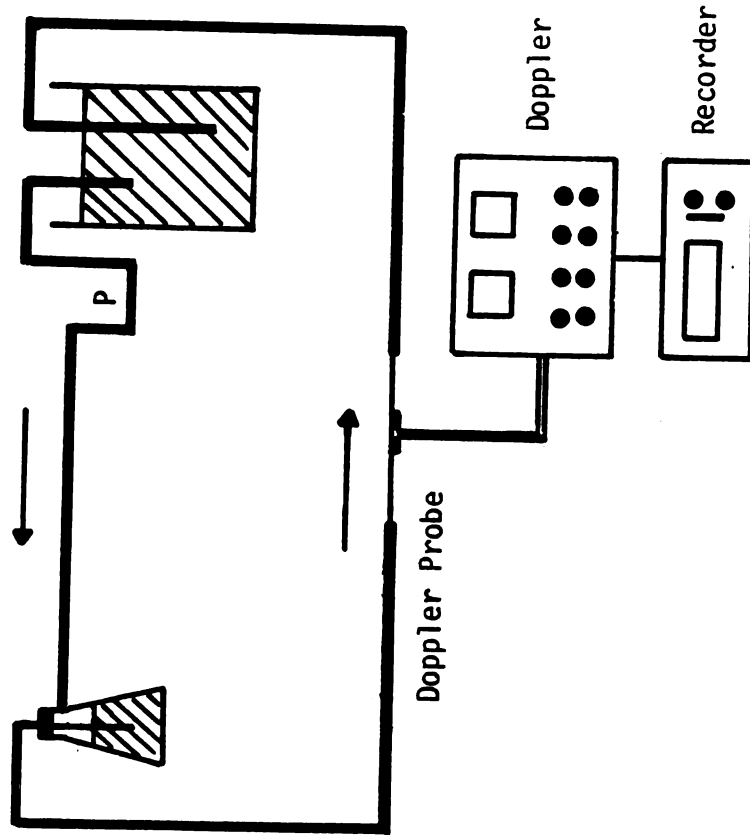
IN VITRO SYSTEM FOR DOPPLER STUDIES

FIGURE 6

Whole milk was used for all in vitro studies because the reflection characteristics of the homogenized fat particles in milk were considered to be similar to the reflection characteristics of erythrocytes in blood (Forsberg and Olin, 1980). All studies were performed with milk at room temperature ($25\text{-}28^{\circ}$ C). Volume in the Erlenemeyer flask was held nearly constant at 1.6 liters to suppress pulsatile flow through the circuit. The use of the closed flask provided relatively non-pulsatile flow past the Doppler probe site as a result of the compliant air space in the Erlenemeyer flask. Consequently, high quality Doppler signal was obtained at all flow velocities studied. The total volume of the circuit was 6.0 L.

In Vitro Pump Calibration

Pump calibration was performed at the beginning and end of each study day. The protocol was to set the pump speed, allow stabilization of flow for 30 seconds, and the obtain 2-3 timed volumetric collections of greater than 25 seconds each using a digital stopwatch and graduated cylinder. A mean flow rate was calculated for each pump setting for that day. The flows studied ranged from 104 to 820 ml/min. All data were submitted to linear regression analysis of volumetric flow, ml/min, on pump tachometer setting.

In Vitro Doppler Evaluation

The mean voltage-velocity relationship was studied using the circuit shown in Figure 6. After completion of the pump calibration, a 15° angle flat Doppler probe (Parks Electronics, Beaverton, OR) with a nominal frequency of 9.3 mHz was placed facing oncoming flow and secured

over the Latex cuff. Contact with the silastic segment was through
Aquasonic gel (Smith, Kline Instruments, Inc., Sunnyvale, CA). The probe
was adjusted while milk was pumped through the circuit past the probe site
until maximum audio and meter signal were obtained. The Doppler shift
was converted to mean voltage by the Doppler Model 806A (Parks Electronics,
Beaverton, OR) and output recorded on the Rl-5D.C.P. recorder (Parks
Electronics, Beaverton, OR). The Doppler 806A is a bi-directional
Doppler with a number of output modes. The mean velocity setting was
used for all velocity recordings. The oscillator frequency was set for
the probe frequency. The demodulator and zero-crossing channels were set
according to operating instructions. The Rl-5D.C.P. recorder was zeroed
according to operating instructions and set on a scale deflection of
10 mV/mm except at high flow rates when 20 mV/mm was required to remain
on paper scale.

After probe placement was complete, the pump was stopped and a
background recording made. Following this, the pump tachometer was set,
flow established and a Doppler recording made for that flow rate. The
pump speed was increased to the next desired setting and after stabilization
of the new flow rate, the Doppler output was recorded. This process was
repeated for each of the pump settings used for the previous pump
calibration. In 6 studies, measurements were made as the pump speed was
incrementally increased. In 4 studies, measurements were made as pump
speed was varied first in ascending and then descending increments of
flow over this range. Doppler output signal was recorded at a chart
speed of 5 mm/sec for a total of 20-30 seconds at each pump setting.
In each study, data was obtained over the total range of flow rates

(approximately 100-800 ml/min). A sample recording is shown in Figure 7.

To evaluate linearity at less than maximum signal, the probe position was varied to reduce voltage output for comparison to maximum signal. The recording procedure was then repeated using the protocol described above.

Five studies were performed using whole milk and five studies were performed using a combination of whole milk (5.0 L) and whipping cream (1.0 L). This modification was designed to augment fat content of the medium. It was thought that by increasing the number of fat particles available to reflect the Doppler signal, the signal output would be enhanced. Since no difference was measured, all data were combined.

The Doppler recording was analyzed by division of the recording for a given flow velocity into 25 mm increments (equal to 5 seconds) and calculation of a mean voltage for each of these increments for a total of at least 3 values for each pump setting. An overall mean voltage for a given pump setting was calculated from these individual increments. The background value was subtracted and this value used as the voltage output for that respective flow rate.

To convert volumetric flow in ml/min to cm/sec, the cross-sectional area of the silastic segment was measured and used to calculate the actual linear velocity for each volumetric flow rate. This was calculated from the measured length and volume of that tubing segment. These data were used to calculate cross-sectional area as follows:

$$\text{Cross-sectional area, cm}^2 = \frac{\text{Volume, ml}}{\text{Length, cm}}$$

The conversion of ml/min to cm/sec then utilized the equation:
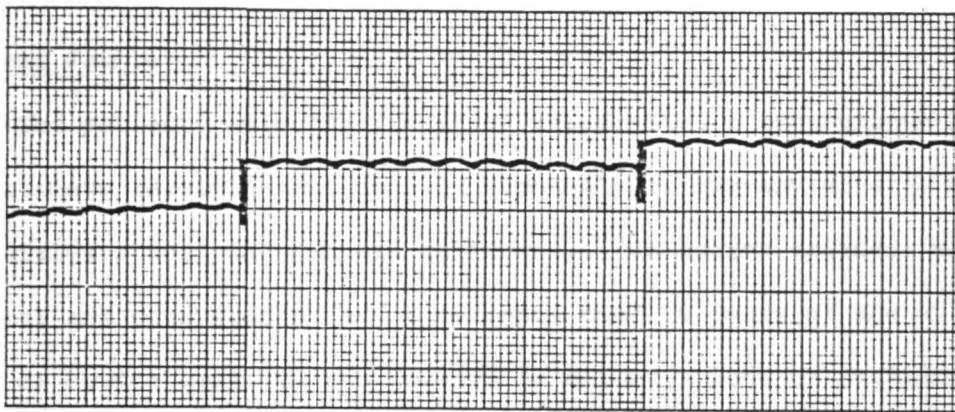
DOPPLER RECORDING AT 3 IN VITRO MILK FLOW RATES

FIGURE 7

$$\text{Linear velocity, cm/sec} = \frac{\text{Flow Rate, ml/min}}{60(\text{Cross-sectional area, cm}^2)}$$

The actual cross-sectional area of the silastic segment used for these studies was 0.167 cm^2. All Doppler studies were subjected to linear regression analysis of voltage output on linear flow velocity.

In Vivo Studies

Patient Sample

The patients selected for study represented a convenience sample of patients receiving maintenance hemodialysis therapy at a 17 station hemodialysis unit in Northern California. Selection criteria were minimal and consisted of adult patients over 18 years of age with a PTFE or Bovine graft in the forearm in either a loop or straight configuration. All grafts had been in place for greater than three months. Twelve patients were studied with five patients studied two or more times. Informed consent was obtained from all patients studied. A total of 30 Doppler studies were done.

In Vivo Pump Calibration

For those patients selected for study, a predialysis blood pump calibration was performed with the extracorporeal circuit to be used for the dialysis treatment. Consequently, a variety of blood pumps were used for these studies. Normal saline was used for all calibration studies. Pump speeds were selected to provide volumetric flows ranging from 57 to 471 ml/min, with a minimum of 3 flow rates studied with each calibration. The pump speed was set, flow allowed to stabilize for 15 seconds and timed collections performed, using a digital stopwatch and a graduated

cylinder. Collection times were determined to 0.01 seconds. At least

2 timed collections at each pump setting were done, with collection

volumes designed to achieve collection times greater than 22 seconds to

minimize operator error. Volumetric flows were calculated for each

collection and a mean flow rate was determined for each pump speed

studied. The pump speeds used for the pump calibration were then used

for the subsequent Doppler measurements.

In Vivo Doppler Measurement

Patient weight and supine blood pressure were measured and recorded

predialysis. Fistula needles (15 gauge) were placed in the vascular access

graft at least 3 inches apart, with the arterial and venous needles

directed toward the respective anastamoses. Dialysis was initiated

according to standard procedure. The patient's arm was positioned below

heart level to maintain optimal filling of the graft. A site between the

needles was selected for probe placement, contact gel was applied, and the

Doppler 15° angle flat probe was positioned with the crystals oriented

toward oncoming flow. The probe was adjusted until maximum audio and meter

signal was obtained while the extracorporeal circuit was operated at

the prescribed blood flow rate. The probe was secured with tape to

prevent movement of the probe once optimal placement was identified.

Figure 8 is a schematic representation of the flow circuit and Doppler

probe placement.

After securing the probe placement, the blood pump was stopped,

flow through the graft was allowed to stabilize for approximately

30 seconds and a recording made of the Doppler signal representing

total graft flow. The signal was recorded for at least 15 seconds or
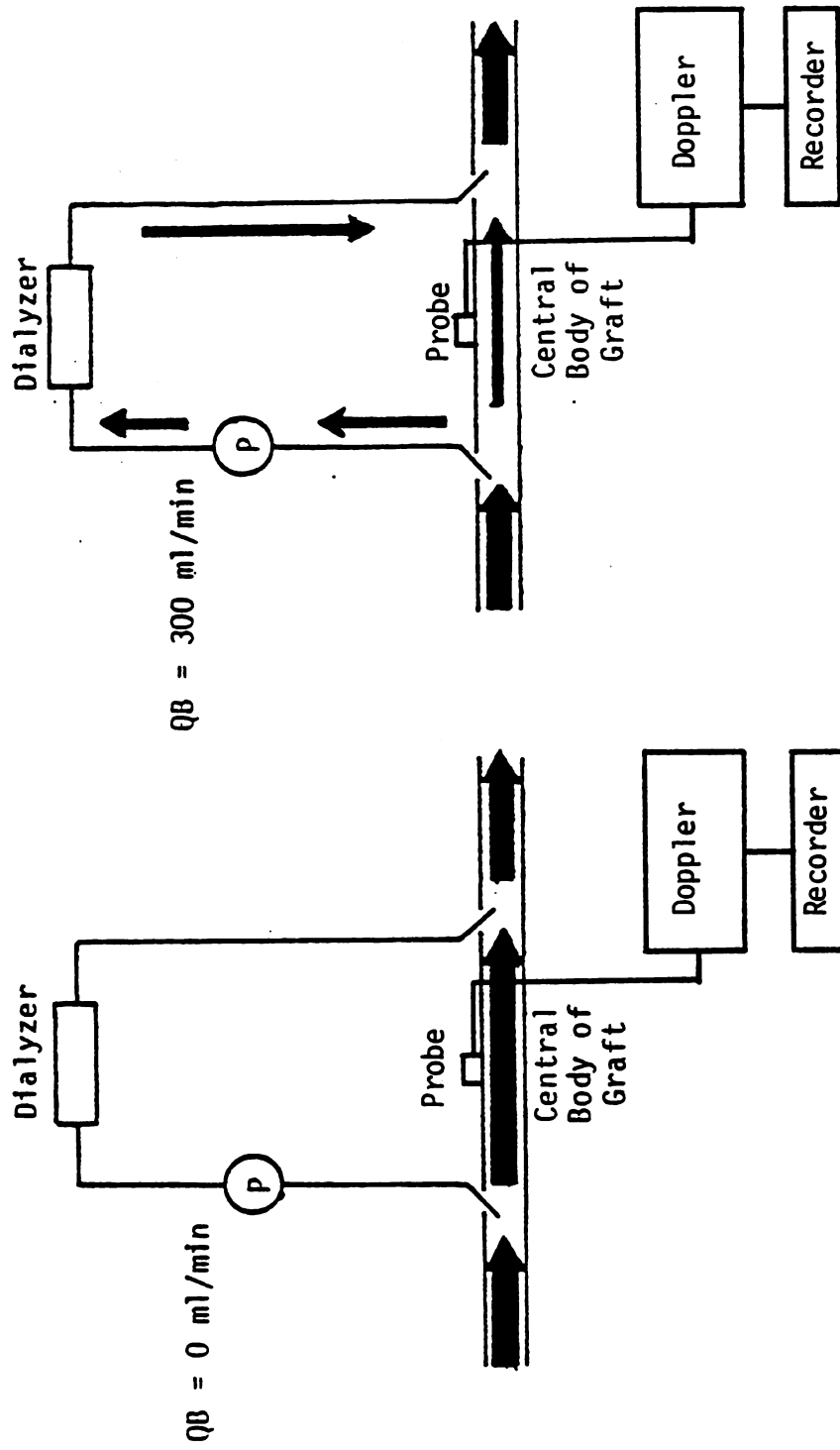
IN VIVO CIRCUIT FOR DOPPLER STUDY

FIGURE 8

until the recorded value was stable. Once this value was obtained, the first pump speed was set, the pump started and allowed to stabilize for 15 seconds. Then, the Doppler signal for this flow was recorded for at least 15 seconds. This procedure was repeated for the 3-4 pump speeds studied for the predialysis blood pump calibration. The flow rates were studied in ascending order. At the completion of the study, the blood pump was stopped, blood flow through the graft allowed to stabilize and the arterial anastamosis manually occluded. Audio signal was followed until flow stopped and a recording was then made to obtain the background signal. The recording was completed, identified by patient code and the operating parameters of the Doppler noted. The probe was then removed. A sample recording is shown in Figure 9.

Nine patients were also studied within 45 minutes before the termination of dialysis using the same Doppler protocol described above. In 3 patients, the second study was not done because of technical or patient complications which prevented restudy. At the time of the second intradialytic Doppler evaluation, blood pressure was measured and the total ultrafiltrate (QFT) removed was estimated. The QFT was calculated as the fraction of the total weight loss that had occurred at the elapsed time of dialysis (ETD) when the last Doppler evaluation was done. All Doppler recordings were analyzed using the analysis protocol described earlier in the in vitro methods section. These data were subjected to linear regression analysis of mean Doppler voltage as a function of blood flow rate through the dialyzer circuti (QB).

Graft flow (Qg) was calculated for each Doppler study from the linear regression equation as follows:
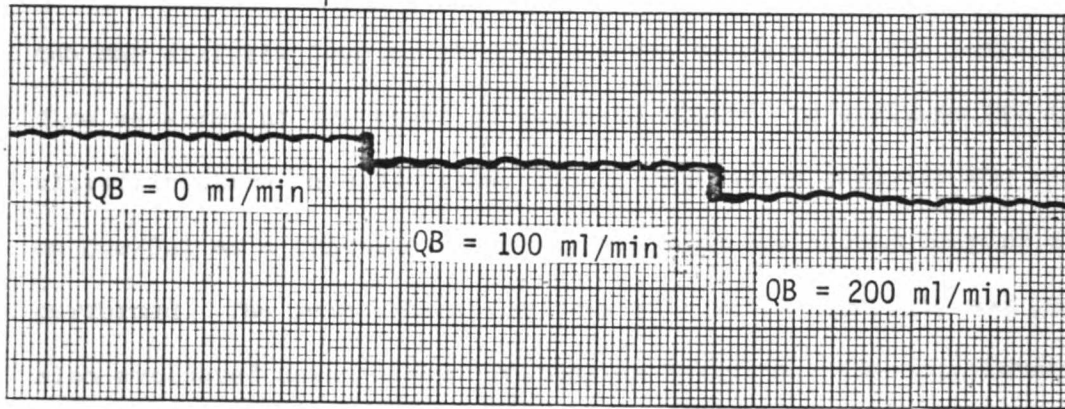
SAMPLE RECORDING OF IN VIVO DOPPLER STUDY

FIGURE 9

Doppler voltage (v) = a - b(QB)

Thus when voltage equals zero, which by definition means total graft

flow is diverted through the dialyzer circuit and QB = Qg

0 = a - b(QB)

Therefore

$$QB = \frac{a}{b} = Qg$$

For the paired intradialytic measurements, graft flow calculated from

the end dialysis Doppler study (Qge) was compared to the initial graft

flow measured at the start of dialysis (Qgi). To evaluate the effect of

ultrafiltration on graft flow, linear regression analysis was performed

on Qge/Qgi as a function of QFT at the time the second Doppler study was

performed. The relationship between this ratio (Qge/Qgi) and Qgi was

also evaluated using linear regression analysis. The relationship between

mean arterial pressure, calculated from the blood pressure measurements

at the time of the intradialytic Doppler studies, and Qge/Qgi was

statistically evaluated.

Isotope Studies

To establish validity of the Doppler technique, the isotope infusion

method described by Kaye and co-workers in 1977 was used to determine

volumetric graft flow. The infusion studies used pertechnetate, a

technecium-labeled compound commonly used for organ imaging. Pertechnetate

distributes in the body similarly to the iodide ion but is not organified

when trapped in the thyroid gland. It concentrates in the thyroid gland,

salivary glands, stomach and choroid plexus. After intravenous administration,

it remains in the circulatory system for sufficient time to permit organ perfusion and major vessel studies, in addition to quantitation of vascular volumes. Pertechnetate is considered an ideal isotope since the half-life is about 6 1/2 hours (MIRD Pamphlet) and the total dose given for these infusion studies was approximately 100 microcuries.

A 70 kilogram patient receiving the maximum dose for organ perfusion of 20 millicuries would be expected to receive an absorbed radiation dose of 12 rads to the thyroid gland. Large bowel and stomach doses are estimated at 2.94 and 2.14 rads respectively for the same dose. For these infusion studies in dialysis patients in which approximately 100 microcuries were administered, the estimated maximum absorbed radiation doses were estimated at 0.0147 and 0.0107 rads respectively.

The rate at which the radioisotope was infused in these dialysis patients was 30-70 microcuries per minute. It was expected that the minimum vascular access graft flow in these patients would be 400 ml/min. Thus the maximum concentration of isotope at the point of entry was estimated to be 70/400 or 0.175 microcuries/ml of whole blood. Upon reaching equilibrium with an average total blood volume of 5.0 L, the maximal vascular concentration would be 0.020 microcuries/ml of whole blood. For comparison, administration of 20 millicuries of pertechnetate for organ perfusion studies would result in a vascular concentration of 4 microcuries/ml of whole blood.

Patient Sample

Informed consent was obtained from all patients studied. Five patients, 4 males and 1 female, were studied and all patients had 1 or

more Doppler evaluations of graft flow rate prior to the day of the infusion study. Four of the five grafts studied were PTFE and 1 was a Bovine heterograft. Two of the PTFE grafts were in a forearm loop configuration while the remaining 3 patients had straight forearm grafts. All patients were >50 years of age and all grafts had been in place for longer than 1 year.

The protocol required that a Doppler study be done just prior to the infusion study. This would allow direct comparison under similar physiologic conditions. A predialysis pump calibration was performed for the Doppler evaluation using the protocol previously described. The patient's predialysis weight and supine blood pressure were recorded. Fifteen gauge fistula needles were placed as close to the respective anastamoses as feasible and both needles were directed toward the respective anastamoses. Dialysis was initiated. At an elapsed time of dialysis ranging from 1-3 hours, depending on the availability of infusion pump and isotope, a Doppler study was done using the standard Doppler protocol described earlier. Upon completion of the Doppler assessment, the extracorporeal circuit was disconnected from the patient and was recirculated while the infusion study was performed (<15 minutes). A 19 gauge butterfly needle was inserted into the afferent limb of the graft, approximately 1 inch from the arterial needle and, in the first 2 studies, directed away from the arterial anastamosis. In 3 studies, this needle was placed in the same orientation as the arterial fistula needle to obtain optimum mixing of infusate in blood. This needle was used as the infusion site for the pertechnetate. Both fistula needles were fitted with 3-way stopcocks to facilitate sampling. This schema

is shown in Figure 2 dispalying needle placement, infusion and sampling

sites. The infusate consisted of pertechnetate in normal saline and

was prepared by the Nuclear Medicine Department. Actual pertechnetate

concentrations ranged from 1.15 to 1.90 microcuries/ml of saline. The

infusion rate was set at 34 ml/min and a MedRad Pump (MedRad, Inc.,

Pittsburgh, PA) was used to infuse the pertechnetate. Volumetric

calibration of this pump was checked on 2 occasions and the actual

volumetric infusion rate at the pump setting of 34 ml/min was found to be

34.37 ± 0.38 ml/min ($M \pm 2SD$, N=4). The infusion pump and digital stopwatch

were started simultaneously. Four ml samples were drawn simultaneously

from the arterial and venous sampling sites at 20, 40, 60 and 80 seconds

elapsed time after withdrawing 6 ml of blood from the other stopcock

sidearm to insure that a fresh systemic sample was obtained. This blood

was returned to the patient via the stopcock after each sample. At the

end of the sample period, (80 seconds), the infusion was terminated and

the extracorporeal circuit was re-established. The blood samples and

remaining infusate were submitted to the Nuclear Medicine Department for

counting and disposal. Two ml samples were counted in a commercial well

counter (Squibb and Sons, Inc., Princeton, NJ) and duplicate dilutions

of 1:50 were made of the infusate. The samples were counted for 10 or

40 seconds depending on the actual counting rate to avoid freezing the

counter.

Actual graft flow rate was calculated using the following equation:

$$\text{Graft flow, ml/min} = \frac{\text{Counts infused/min}}{\text{Venous counts/ml} - \text{Arterial counts/ml}}$$

No patient complications from this procedure were observed.

CHAPTER 4

RESULTS

In Vitro Pump Calibration

The results of all 7 pump calibrations are shown in Figure 10. Volumetric flow expressed as ml/min is plotted as a function of pump tachometer setting (dimensionless). Each data point represents the mean of 5-14 timed collections. The solid line represents the results of linear regression analysis of all flow rates studied. The broken lines enclose the 95% confidence limits for these data. The data points are plotted as mean and 2 SD. The slope of the line is defined by the equation:

$$y = 11.89X + 8.36 \pm 34.15$$

The correlation coefficient was 0.998. Two standard deviations of the means ranged from 3-8% with the largest variability occurring in the lower flow rates. The dual pump headers created resistance to pump action such that these flow rates were difficult to study because of circuit breaker activation. Therefore, fewer calibrations and Doppler recordings were done at flow rates less than 14.3 cm/sec. To maximize accuracy for the Doppler studies, the mean calculated for the pump calibrations performed on the same day were used as the flow rates for the respective Doppler studies since the coefficient of variation on the daily pump calibrations did not exceed 5% at all volumetric flows. This was felt to be the optimal approach for evaluating the Doppler voltage-velocity relationship. The means and standard deviations of all pump

$$y = 11.89X + 8.36 \pm 34.15$$
$$r = 0.998$$
$$N = 7$$

IN VITRO PUMP CALIBRATIONS
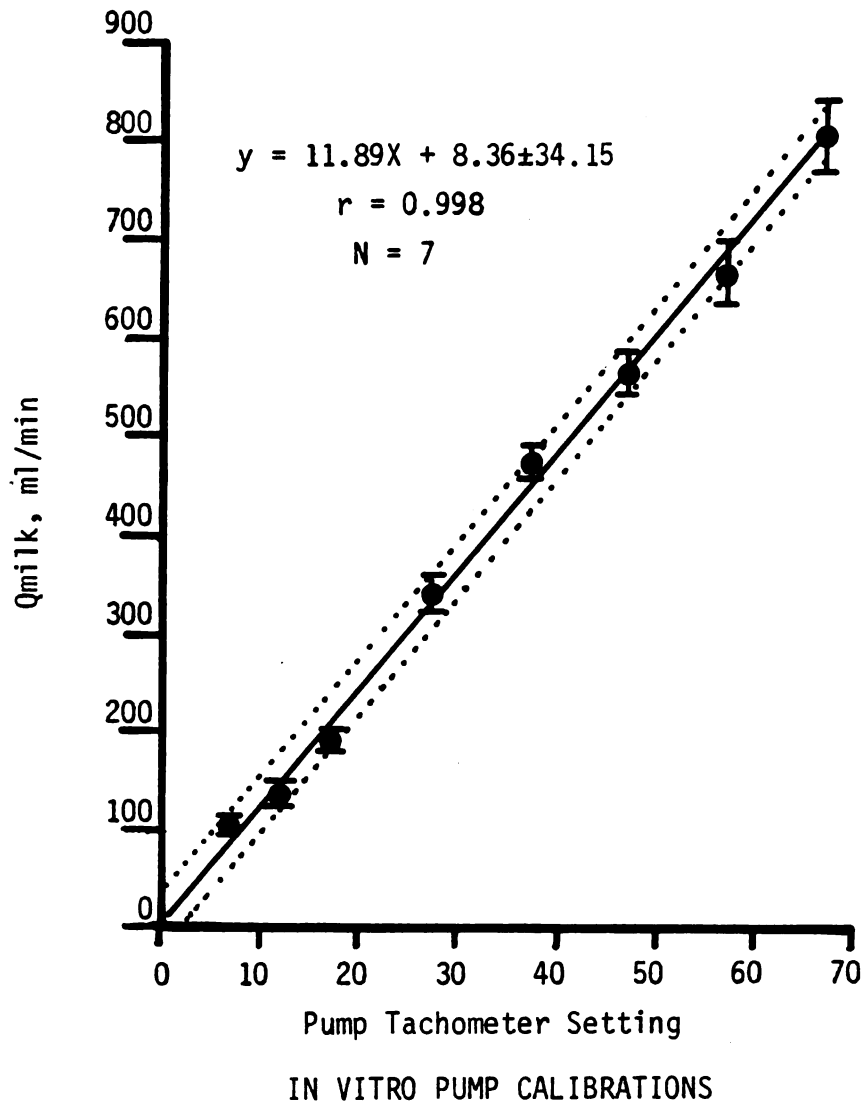
FIGURE 10

calibration studies are shown in Table I.

In Vitro Doppler Studies

The results of the in vitro Doppler studies are shown in Figure 11 where mean Doppler signal in volts (v) is plotted as a function of milk velocity (Qmilk) in cm/sec. Measured flow velocities ranged from 5.19 to 82.93 cm/sec. To achieve a linear velocity of less than 14 cm/sec a single pump header was used in 1 study.

The slopes of the individual studies ranged from 0.00764 to 0.0182 and the data are available in Table II. All studies were linear with correlation coefficients ranging from 0.992 to 0.999. The linearity of these data was not affected by the actual slope. This finding implied that even if less than maximum signal was obtained in vivo, the mean voltage-velocity relationship should remain linear. This had important implications for the in vivo application of this technique. Variable skin thickness and tissue over the graft as well as depth of the graft could influence Doppler voltage in that signal would be attenuated as a function of these variables. The actual clinical conditions of needle placement and available space over the graft for the Doppler probe might preclude optimal positioning of the probe for maximal signal. For the paired studies, it would not be necessary to achieve the exact same probe position for the second intradialytic Doppler study. These data indicated that there would be a linear relationship of voltage to flow velocity over a wide range of slopes.

The ten studies demonstrated a mean positive intercept of 0.046 volts, with a range of 0 to 0.087 and was independent of slope. One interpretation

TABLE I

IN VITRO PUMP CALIBRATION

Pump Setting	N	Volumetric Flow ml/min M ± 2SD
7	5	106.0 ± 2
12	6	139.2 ± 10.4
17	14	193.2 ± 10.4
27	14	343.5 ± 15.9
37	14	477.0 ± 16.0
47	14	566.1 ± 24.5
57	14	666.5 ± 30.6
67	14	805.8 ± 38.8
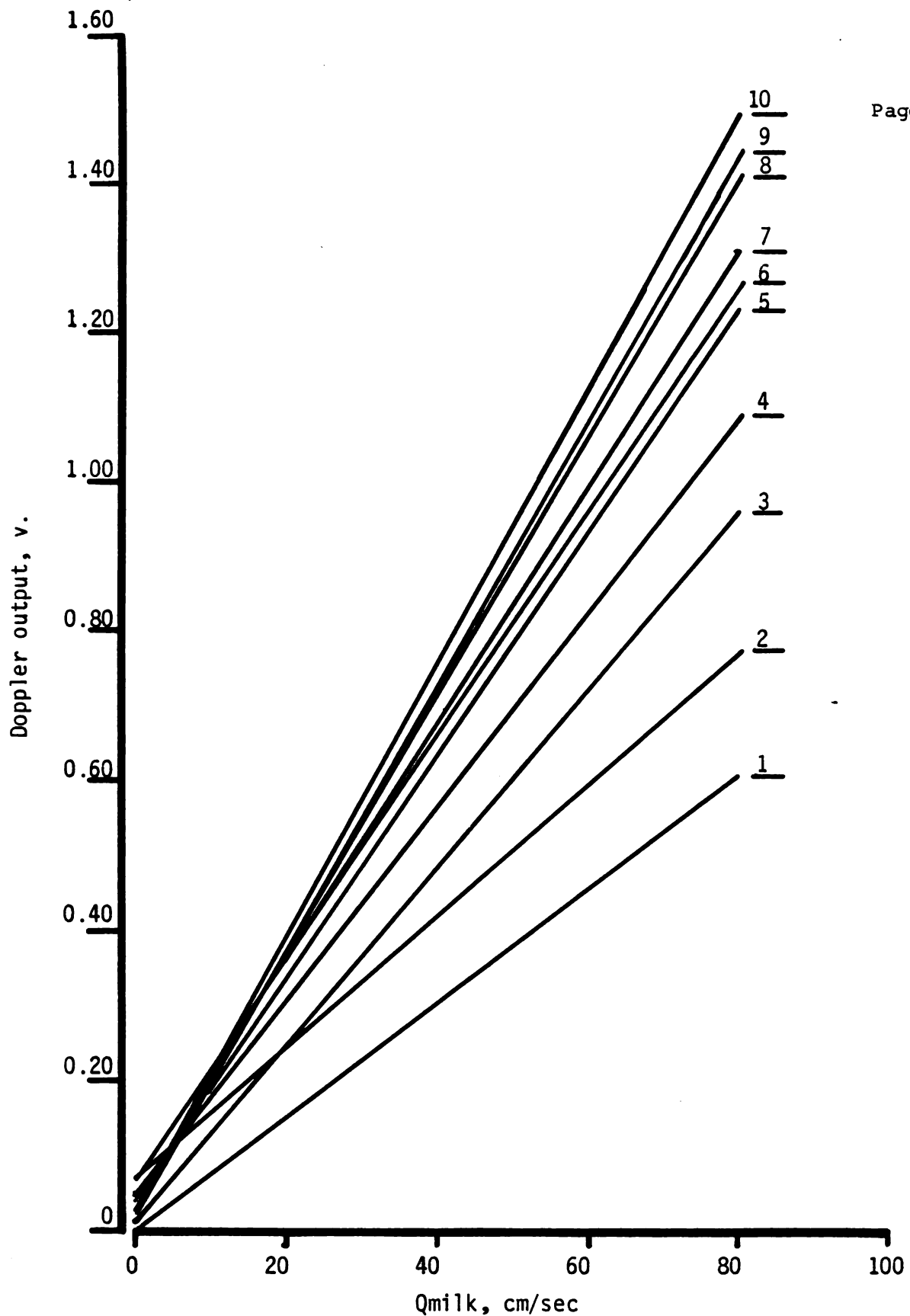
IN VITRO DOPPLER STUDIES

FIGURE 11

TABLE II

IN VITRO DOPPLER STUDIES

Study #	N Observations	Slope	Intercept	r
1	7	0.00764	0.000	0.992
2	7	0.00859	0.087	0.997
3	7	0.01181	0.017	0.997
4	9	0.01290	0.058	0.999
5	7	0.01459	0.061	0.999
6	8	0.01472	0.076	0.998
7	13	0.01564	0.057	0.998
8	13	0.01716	0.031	0.999
9	13	0.01742	0.036	0.999
10	13	0.01815	0.041	0.999

of this finding is that the Doppler is non-linear below a flow velocity

of 14 cm/sec. It has been reported that the Doppler is not linear at

the low and very high ends of the velocity range (Shoor et al, 1979).

The single study evaluating flow velocity below 14 cm/sec was linear but

with an intercept of 0.0583 volts. The cause of this intercept remains

obscure but may reflect the suboptimal angle of the 15° angle probe. If

the non-linearity of the Doppler is true, this would result in the Doppler

overestimating volumetric flow in vivo, since the in vivo analysis was

based on the assumption that Doppler remain linear to zero. The in vivo

Doppler study measures voltage output at high velocities and is then

extrapolated to zero. Assuming Doppler voltage is non-linear in vivo

at low velocity, these data would have to be corrected for the average

in vitro intercept.

In Vivo Doppler Studies

A total of 30 Doppler studies were performed representing a patient

population of 12. Nine of the 12 patients had paired Doppler studies

performed at the beginning and end of dialysis to evaluate change in graft

flow during dialysis. The results of all Doppler studies are shown in

Table III. This Table includes patient number, number of flow rates

studied, slope, y intercept corrected for the average in vitro intercept

of 0.046, and calculated graft flow with 2 SD and r values for each

study. The graft flows ranged from 550-1599 ml/min. The results were

linear with r values ranging from 0.958 to 0.999. Table IV compares

the calculated graft flows for the Doppler studies uncorrected for in

vitro intercept and the Doppler studies corrected for the intercept value.

TABLE III

IN VIVO DOPPLER STUDIES

Pt. #	Date	N Flows	y Intercept ± 2SD	Slope	r	Qg 2SD ml/min
1	8/31/84	5	0.83 ± 0.04	-0.00057	0.985	1460 ± 63
2	8/31/84	5	0.48 ± 0.03	-0.00039	0.965	1228 ± 79
		4	0.63 ± 0.02	-0.00080	0.997	788 ± 24
3	10/10/84	4	0.54 ± 0.01	-0.00069	0.999	783 ± 14
		4	0.45 ± 0.04	-0.00062	0.977	733 ± 66
4	10/12/84	4	0.78 ± 0.01	-0.00102	0.999	769 ± 12
		4	0.68 ± 0.06	-0.00100	0.987	680 ± 57
	3/6/85	5	0.85 ± 0.03	-0.00108	0.997	785 ± 26
	3/29/85	5	0.96 ± 0.03	-0.00153	0.998	627 ± 21
5	1/14/85	5	0.48 ± 0.05	-0.00063	0.974	767 ± 76
		5	0.42 ± 0.05	-0.00068	0.967	616 ± 78
	2/7/85	4	0.35 ± 0.03	-0.00060	0.981	588 ± 53
	2/18/85	4	0.53 ± 0.01	-0.00070	0.999	760 ± 21
		4	0.40 ± 0.01	-0.00064	0.999	623 ± 16
	3/1/85	5	0.57 ± 0.03	-0.00095	0.997	603 ± 27
6	1/17/85	4	1.02 ± 0.01	-0.00067	0.999	1511 ± 17
	3/19/85	5	0.66 ± 0.01	-0.00041	0.997	1599 ± 25
	3/21/85	5	1.36 ± 0.03	-0.00112	0.997	1212 ± 27
7	1/28/85	4	1.08 ± 0.04	-0.00161	0.997	672 ± 23
8	2/11/85	4	0.54 ± 0.02	-0.00038	0.989	1433 ± 43
		4	0.52 ± 0.01	-0.00041	0.993	1261 ± 35
	4/3/85	5	0.49 ± 0.03	-0.00037	0.958	1322 ± 94
9	2/14/85	4	0.59 ± 0.01	-0.00043	0.995	1369 ± 29
		4	0.58 ± 0.02	-0.00057	0.993	1019 ± 35
10	2/20/85	5	0.55 ± 0.01	-0.00075	0.998	738 ± 19
		5	0.64 ± 0.04	-0.00116	0.995	550 ± 31
11	2/22/85	4	0.74 ± 0.03	-0.00077	0.990	963 ± 45
	4/10/85	5	0.64 ± 0.01	-0.00059	0.999	1081 ± 14
12	4/4/85	5	0.64 ± 0.02	-0.00056	0.996	1150 ± 36
		5	1.16 ± 0.04	-0.00107	0.997	1080 ± 34

TABLE IV

GRAFT FLOW CALCULATED FROM DOPPLER EVALUATION

| Pt. #	Uncorrected For Intercept	Corrected For Intercept
1	1541	1460
2	1346	1228
	846	788
3	849	783
	807	733
4	814	769
	726	680
	827	785
	656	627
5	840	767
	684	616
	665	588
	825	760
	695	623
	651	603
6	1579	1511
	1712	1599
	1252	1212
7	701	672
8	1554	1433
	1373	1261
	1447	1322
9	1476	1369
	1100	1019
10	799	738
	589	550
11	1023	963
	1159	1081
12	1233	1150
	1123	1080

Figure 12 shows an analysis of the ratio of the end dialysis graft flow over the initial graft flow (Qge/Qgi) from the paired studies as a function of the total quantity of ultrafiltrate (QFT) at the time the second Doppler study was performed. A statistically significant correlation (p<0.05) was found between the decrease in graft flow during dialysis and the total ultrafiltrate removed during the same period. The total number of studies is small but the relationship does suggest that, as total ultrafiltrate increases, graft flow will diminish. These data are available for inspection in Table V.

No statistically significant relationship was found between the change in graft flow and the initial graft flow. The relationship between mean arterial pressure calculated from blood pressure measurements at the time of the intradialytic Doppler studies and Qge/Qgi was examined and no statistically significant correlation was found.

Isotope Measurements

Table VI contains the data obtained from the isotope studies used to validate the Doppler technique. Included in this Table is patient number, the number of isotope determinations, the graft flow calculated from the isotope measurements and the corresponding graft flow calculated from the Doppler technique. As discussed earlier, the Doppler value was corrected for the average in vitro intercept of 0.046 volts.

Figure 13 shows the results of comparison of graft flow rates calculated from Doppler measurements and isotopic examinations. The Doppler flow rate is shown on the ordinate while the flow rate determined from the isotope measurements is shown on the abscissa. The solid line

$$y = -0.0931x + 0.9855 \pm 0.145 \text{ (M+2SD)}$$
$$N = 9, \ r = 0.72 \quad p<0.05$$
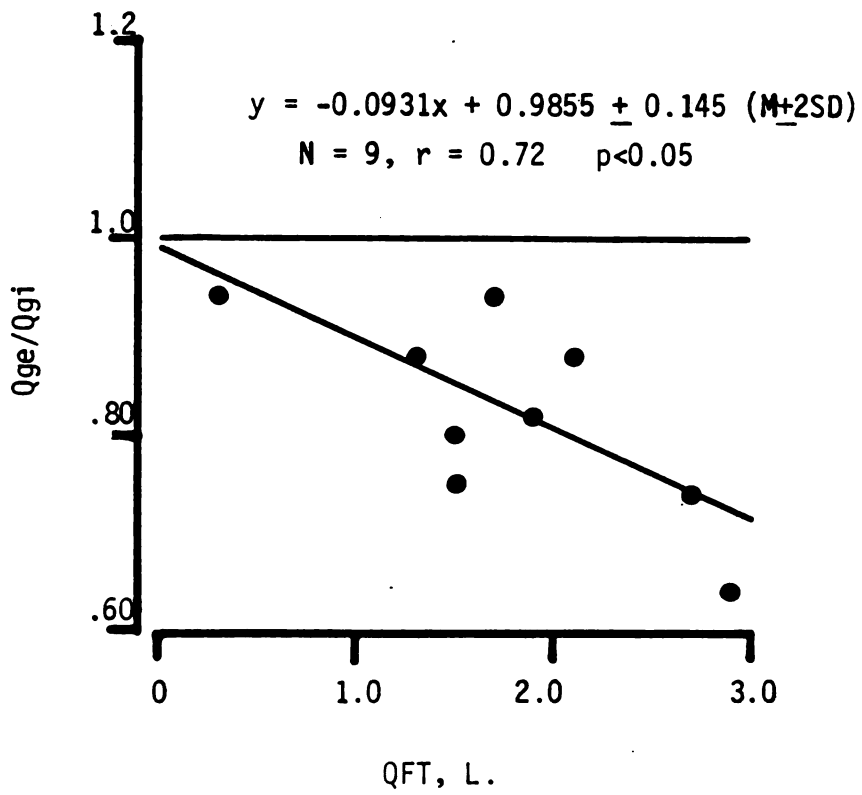
EFFECT OF ULTRAFILTRATION DURING DIALYSIS
ON GRAFT FLOW RATE

FIGURE 12

TABLE V

PAIRED IN VIVO DOPPLER STUDIES

EFFECT OF ULTRAFILTRATION (QFT)

Pt. #	Time of Dialysis Hrs.	QFT, L.	Qg, ml/min M ± 2SD	Qg end / Qg initial
2	0.18	0	1228 ± 79	
	3.0	2.9	788 ± 24	0.64
3	0.25	0	783 ± 14	
	2.0	1.7	733 ± 66	0.94
4	0.25	0	769 ± 12	
	2.25	1.3	680 ± 57	0.88
5	0.25	0	767 ± 76	
	2.25	1.5	616 ± 78	0.80
8	0.18	0	1433 ± 43	
	2.50	2.1	1261 ± 35	0.88
9	0.18	0	1369 ± 29	
	2.50	2.7	1019 ± 35	0.74
5	0.25	0	760 ± 21	
	2.50	1.9	623 ± 16	0.82
10	0.25	0	738 ± 19	
	3.0	1.5	550 ± 31	0.75
12	0.25	0	1150 ± 36	
	3.0	0.3	1080 ± 34	0.94

TABLE VI

PERTECHNETATE STUDIES

Patient #	Date	N Samples	$Qg \pm SD$ ml/min Isotope	$Qg \pm SD$ ml/min Doppler
5	3/1/85	4	659 ± 98	603 ± 14
6	3/21/85	3	1311 ± 70	1212 ± 14
4	3/19/85	2	574 ± 41	627 ± 11
8	4/3/85	4	1222 ± 26	1322 ± 47
11	4/10/85	4	1119 ± 143	1081 ± 7

$$y = 0.969X + 27.74 \pm 184.95$$
$$N = 5 \quad r = 0.97 \quad p<0.005$$
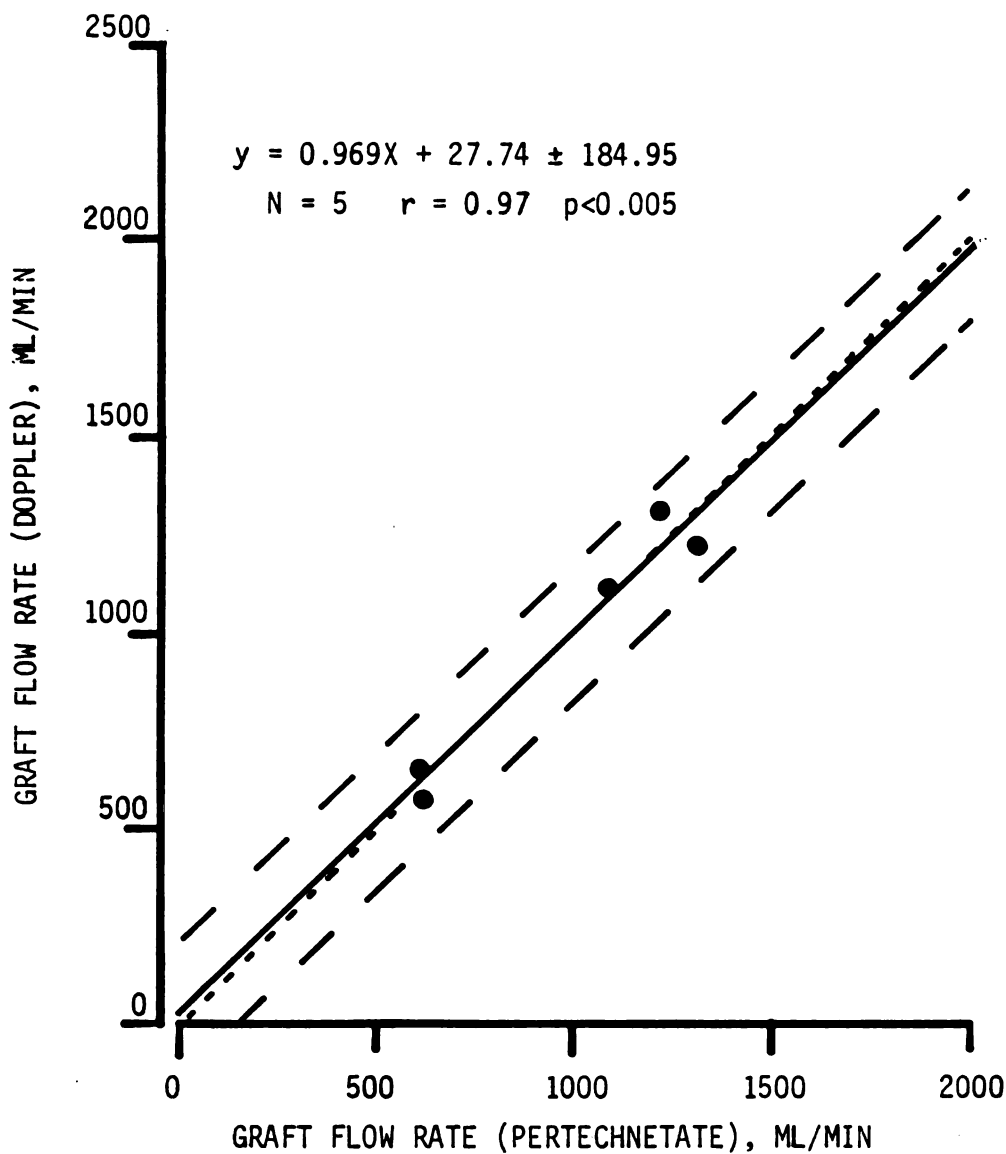
COMPARISON OF GRAFT FLOW RATES MEASURED BY
PERTECHNETATE INFUSION AND DOPPLER

FIGURE 13

represents linear regression of the actual data with 95% confidence

limits shown by the equidistant broken lines. The center interrupted

line is the unity line and indicates that at a graft flow rate of 500 ml/min,

the Doppler technique would overestimate graft flow rate by ∿15 ml/min.

At graft flows of 2000 ml/min, the Doppler technique would underestimate

true graft flow by approximately 25 ml/min. In this sample of patients,

measured graft flows ranged from approximately 574 to 1322 ml/min.

Therefore, the regression line is very close to unity over this range. The

r value of 0.97 indicates good agreement between the two flow measurement

techniques and verifies that the Doppler technique provides an accurate

estimate of total graft flow.

Comparison of Multiple Point VS 2 Point Doppler Graft Flow

With the standard Doppler technique developed, 4 or more dialyzer

circuit (QB) flow rates were studied. This included QB = 0 ml/min when full

graft flow was passing through the central body of the graft, i.e. the

blood pump was off. Although, the time required to perform these multiple

flows was short (∿ 10 minutes), time was required to perform the predialysis

pump calibration for the multiple flows (∿ 15 minutes). To simplify this

procedure, reduce the amount of time required, and therefore make the

technique more suitable for frequent assessment, graft flow was calculated

from 2 flow rates, QB = 0 and the highest QB for that study. Table VII

displays patient number, graft flow calculated from multiple point

regression and graft flow calculated from 2 point regression. Both

calculated flow rates were corrected for the average in vitro intercept.

Figure 14 shows these data with graft flow calculated from 2 point

regression plotted as a function of calculated graft flow from multiple

TABLE VII

IN VIVO DOPPLER STUDIES

GRAFT FLOW CALCULATED FROM
ALL MEASUREMENTS VS 2 MEASUREMENTS

Pt. #	Qg, ml/min All Doppler Points	Qg, ml/min 2 Doppler Points*
1	1460	1389
2	1228	1185
	788	790
3	783	769
	733	777
4	769	779
	680	695
	734	730
	785	787
	627	641
5	767	674
	616	556
	588	563
	760	738
	623	619
	603	613
6	1511	1485
	1599	1595
	1212	1199
7	672	689
8	1433	1484
	1261	1222
9	1369	1344
	1019	993
10	**738**	747
	550	555
11	963	926
	1081	1093
12	1150	1184
	1080	1082

*Zero and maximum points

$$y = 0.986X + 3 \pm 63$$
$$N = 30 \quad r = 0.995 \quad p < 0.001$$
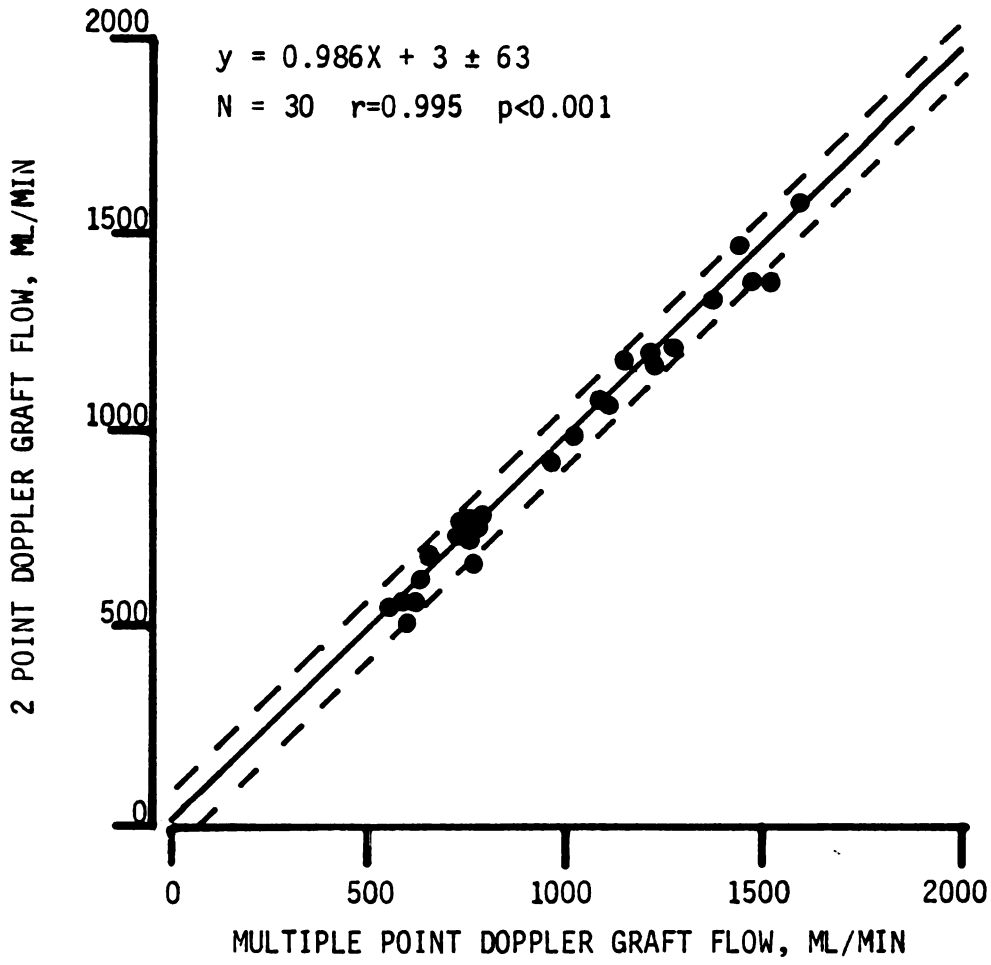
COMPARISON OF GRAFT FLOW CALCULATED FROM MULTIPLE
POINT VS 2 POINT DOPPLER MEASUREMENTS

FIGURE 14

QB measurements. An excellent correlation is seen with an r value of
0.995 (p<0.001). The slope is 0.985 and intercept is 3 indicating almost
a unity relationship over the entire range of study. Therefore, a 2
point Doppler evaluation provides a reliable estimate of total graft
flow and would facilitate the use of this technique.

CHAPTER 5

DISCUSSION

In Vivo Doppler Results

The linear results obtained with this Doppler technique indicates

that the dialyzer circuit can be used to manipulate blood flow through

a vascular access graft and from the derived mathematical relationship,

total graft flow can be quantified. This technique provides a reliable

estimate of graft blood flow without requiring an invasive procedure,

extra patient time or complex equipment, and is suitable for use during

dialysis. Five patients were studied on 2 or more different occasions

(2-5 months between measurements). Despite these variable intervals

between measurements, the variation in the patient-specific data was

less than 15%, indicating stability of graft flow in these patients over

the time span studied.

In grafts with venous outflow stenosis, the time course of diminishing

flow culminating in thrombosis is not known. It could be postulated that

flow may gradually decrease to some critical point at which abrupt

thrombosis occurs. In other situations, flow may continue to decrease to

very low graft flows before thrombosis occurs. In some grafts, the time

course of this process may be affected by other variables, i.e. hypotension,

constriction of the graft, iatrogenic hematoma formation from unsuccessful

cannulation attempts, etc. The ability of this technique to detect a

failing graft remains untested. Repetitive measurements over a short

interval of time may provide more useful information to establish a data

base on graft flow and the variability expected in these measurements.

Pertechnetate Infusion

The pertechnetate infusion studies validated the Doppler evaluation
of graft flow in this study. Graft flow calculated from the infusion
method was more variable between the individual samples than the Doppler
technique. It was difficult to interpret this finding since all cited
references for the method did not report the observed reproducibility of
the method. This finding may represent measurement artifact, inadequate
infusate-blood mixing, the limits of the method's sensitivity, or actual
instantaneous variations in graft flow. The Doppler reflects mean flow
and therefore may dampen flow changes that occur during cardiac systole
and diastole.

The comparison of the mean graft flow from isotope measurements and
Doppler-obtained flow rates were highly correlated (Figure 13). These
results indicated that the non-invasive Doppler technique provides an
accurate estimate of total graft flow.

Consideration was given to correction of the isotopically measured
graft flow rate for the volumetric isotope infusion rate. However, it
was assumed that both graft flow resistance (R, mmHg/ml flow) and the
hydraulic driving force (ΔP across the graft, mmHg) remained constant.
The constant driving force assumption was based on the consideration that
mean arterial pressure minus venous pressure, which determine ΔP, were
unchanged by the short duration and low volume infusion. Prior to the
infusion, the relationship of the hydraulic parameters is given by

$$\Delta P_1 = R_1 Q_{g1}$$

During the infusion the relationship is

$$\Delta P2 = R2(Qg2 + Qi)$$

If ΔP and R remain constant, it follows that $Qg1 = Qg2 + Qi$ and total graft flow is unchanged. A similar assumption must have been made in all the cited studies since in none of these was the graft flow corrected for the infusion rate.

One of the objectives of this study was to look at the effect of intradialytic ultrafiltration on total graft flow as measured by the Doppler method. During dialysis, variable amounts of body water are removed depending on the hydration status of the patient. Ideally, the total quantity of ultrafiltrate should not come from the vascular compartment, but rather plasma refilling from the interstitial compartment should be adequate to maintain vascular volume and therefore maintain blood pressure above hypotensive levels (systolic blood pressure >90 mmHg). If refilling rate is not adequate, vascular volume decreases significantly and hypotension and clinical shock ensue. Fluid shifts between compartments and blood pressure control are complex processes and some data suggests multiple intradialytic factors may influence the fluid shift phenomenon (Gotch, Heineken, Keen, and Evans, 1984). It was beyond the scope of this project to evaluate the effects of these multiple factors on graft flow. However, the Doppler technique provided a method to determine if graft flow changed during dialysis with ultrafiltration. It was of interest to find a statistically significant correlation between the decrease in graft flow during dialysis and the total ultrafiltrate removed during treatment. The sample is small and, because of the

observed variability in Doppler-measured graft flow alluded to earlier,
the clinical significance of these findings cannot be evaluated. If,
however, these results represent true graft flow diminution with
ultrafiltration, marginal graft flow at the start of dialysis might become
inadequate at some point during dialysis if ultrafiltration requirements
are high. This might produce intradialytic recirculation and compromised
therapy. This would impose constraints on extracorporeal blood flow rates,
prevent the implementation of high flux short treatment times, and
require surgical correction.

Multiple Point Doppler Flow VS 2 Point Doppler Flow

The ability to accurately estimate graft flow from measurement of
2 Doppler points (Figure 14) rather than 4-5 points simplifies this
technique. The time required to measure multiple points is ∿10 minutes,
so reducing the number of points would result in a savings in nurse time.
The predialysis pump calibration requires ∿15 minutes to perform. The
technique used for this study determined pump calibration at 3-4 different
pump speeds. If the blood pump to be used during the Doppler study is
shown to be linear, a 2 point calibration should adequate define the
regression of volumetric flow on pump speed. If a 2 point Doppler study
is done, this, then requires pump calibration for only 1 volumetric flow
rate (300-400 ml/min). This would require approximately 1/3 the amount
of time or ∿5 minutes. Another option would be to measure a bubble time
at the selected pump speed (Gotch, 1976) to be used for the Doppler
measurement. This would also result in a time reduction to less than
5 minutes. The third option which would be less desirable, is to rely

on periodic pump calibrations (done monthly or bimonthly) to estimate

the QB at which the modified Doppler measurement is made. This last

option might result in loss of accuracy with the method. Any of these

procedures will result in a reduction of time required to perform a

Doppler evaluation and, therefore, a simplified Doppler estimation of

graft flow. This would make frequent Doppler measurements of graft

flow feasible in a busy clinical setting.

Significance

The results of this study indicate that standard Doppler equipment

can be used to quantitate vascular access graft flow in hemodialysis

patients. The advantages of using this technology in the clinical

setting is that it is non-invasive, inexpensive, portable and can easily

be used by nurses at the time of the patient's regular treatment. Other

quantitative techniques are invasive, costly, require other personnel,

require extra patient time and cannot be used during dialysis to determine

the effect of dialysis on graft flow. To this author's knowledge, the

Doppler technique reported here represents the first simple reliable

method available for use by nurses to quantitatively assess heterologous

vascular access graft flow in hemodialysis patients and appears to be the

only method that can be used to make repetitive measurements during

dialysis.

It is important that graft flow in this patient population be adequate

to achieve therapy goals but not excessive such that the patient is at

risk of high output cardiac failure. Abrupt loss of graft function has

contributed to the morbidity and mortality in this patient population

(Aman et al, 1980). Therefore, the ability to measure and monitor graft

flow over time may be valuable.

The current qualitative nursing assessment has not been adequate to determine whether or not a vascular access graft meets the appropriate requirements for a suitable access. Periodic use of this Doppler technique might identify those grafts in which flow is marginal, declining or excessive. If so, the nurse could initiate remedial action that might reduce the incidence of associated complications and costly hosptializations in these patients.

The in vitro studies showed that the Doppler voltage was linear across the range of flows studied (104-820 ml/min or 5-83 cm/sec). The Doppler principle is based on the fact that the frequency shift is proportional to linear velocity of moving erythrocytes. Shoor et al (1979) reported the results of an in vitro evaluation of Doppler equipment in which Doppler signal was shown as a function of linear velocity ranging from 5-85 cm/sec. These 3 studies which were highly reproducible, were done with the optimum Doppler probe angle. The linear regression equation and correlation coefficient are not reported. This author's linear regression analysis of those data yielded the equation

$$y = 0.0272X + 0.1047 \pm 0.1604 \ (M \pm 2SD), \ N=19, \ r=0.994.$$

The data show a higher slope and higher intercept than those reported here for the in vitro studies. The ten in vitro Doppler evaluations described earlier in this report are the only studies which examined the linearity of the Doppler-velocity relationship across the spectrum of slopes and with less than optimum Doppler probe angle, a condition which may be required when using the technique on patients.

The close correlation of graft flows calculated from multiple

points and that calculated from 2 measurement points indicates that the simple method is accurate for assessing graft flow. This greatly simplifies the Doppler technique without sacrificing accuracy. Consequently, the clinical implementation of this method should be facilitated by this finding.

Limitations

Application of this Doppler technique requires that both fistula needles be placed in a single main channel of a fistula. Therefore, the patient population was restricted to heterologous grafts since they conform to that requirement. Arteriovenous fistulae may have multiple venous channels suitable for cannulation or have one or more branching runoff vessels which occur in close proximity to the arterial anastamosis. Both of these conditions could alter the flow relationships upon which this technique is based. Therefore, the successful application of this technique to surgically created arteriovenous fistulas may not be possible.

If the arteriovenous fistula results in a single main flow channel in which both needles are placed without branching vessels interposed between the cannulation sites, the technique may be appropriate to obtain an estimate of flow. This patient population was not included in this study. The endogenous arteriovenous fistula is also vasoactive vasculature as opposed to the heterologous graft. The ability of this technique to measure fistula flow in the presence of autonomically-induced changes in cross-sectional area remains unknown.

The graft flows studied ranged from 550-1599 ml/min. Assuming a

nominal graft of 6 mm ID, the respective velocities would range from 32-94 cm/sec, exceeding the velocity range studied in vitro (5-83 cm/sec). The maximum graft flow studied with both pertechnetate and Doppler was ∿1300 ml/min, which, with a 6 mm ID graft would be a linear velocity of 77.9 cm/sec. If the cross-sectional area was 0.196 cm^2 (5 mm ID graft), the linear velocity would be 112.2 cm/sec. If there was non-linearity of the Doppler in this range, one would expect that Doppler graft flow would consistently underestimate flow compared to flow calculated from the isotope samples. In one study, the Doppler calcualted value was lower than the isotope while in the other study, it overestimated flow.

The Doppler technique was not evaluated in high flow access grafts (>2000 ml/min). Bouthier et al (1983) found an inverse correlation between graft cross-sectional area and flow velocity. Thus, high graft flows may be more likely to occur in larger cross-sectional area grafts which would produce a lower linear velocity. In view of the fact that no high flow grafts were studied, the ability of this technique to accurately estimate graft flows above 1600 ml/min has not been proven.

The 15° angle flat probe does not achieve the optimal angle for intersecting the blood vessel (Shoor et al, 1979). This is reflected in the low voltage y intercept reported for many of the in vivo studies. An increased probe angle may have boosted the Doppler voltage and, therefore, increased the sensitivity of the method. Despite this methodologic problem, the studies were linear. This probe was used because it simplified placement and could be secured so that position did not change during the course of measurement. The pencil probe would have allowed placement at an optimal angle but maintaining a fixed position with this probe is

impossible without a special holder that is not commercially available. Therefore, the flat probe was selected for these studies.

Implications for Nursing

The ongoing assessment and management of the patient and his/her dialytic therapy is a component of the dialysis nurse's responsibility. A number of patient parameters are assessed using quantitative measures (weight, blood pressure, temperature, etc.). Such an assessment has not been possible with the patient's vascular access, a crucial component of therapy. There has been no satisfactory, simple and objective method of assessing fistula flow to evaluate function. Qualitative nursing assessment techniques have not provided quantitative information about reductions in graft flow which may reflect a stenotic venous outflow tract. Nor can these techniques identify those grafts in which flow is inadequate for hemodialysis or excessive which may affect cardiac function in these patients. Measurement of the actual blood flow rate through a vascular access graft has required subjecting the patient to invasive radiologic or isotopic examination.

This technique could provide a tool which could augment the nursing assessment by providing an easily obtained, accurate measure of graft flow. Frequent interval measurements would give the nurse a data base on graft flow rate. Significant change in subsequent measurements could provide objective data for the nurse and assist in the decision-making process for remedial action.

As stated earlier, complications associated with the patient's vascular access continue to be responsible for a large number of hospital admissions for hemodialysis patients. The implementation of a quantitative

graft assessment technique might be successful in reducing the incidence
of emergency hospitalizations related to these events.

Future Research

The Doppler technique appears to accurately measure heterologous
vascular access graft blood flow. Future research should be directed
toward: (1) Increasing the number of heterologous grafts evaluated using
this technique; (2) periodic measurment of graft flows in a group of
patients in an attempt to detect changes that warrant action to avoid
thrombosis; (3) evaluation of the technique in arteriovenous fistulas
using the conditions described earlier.

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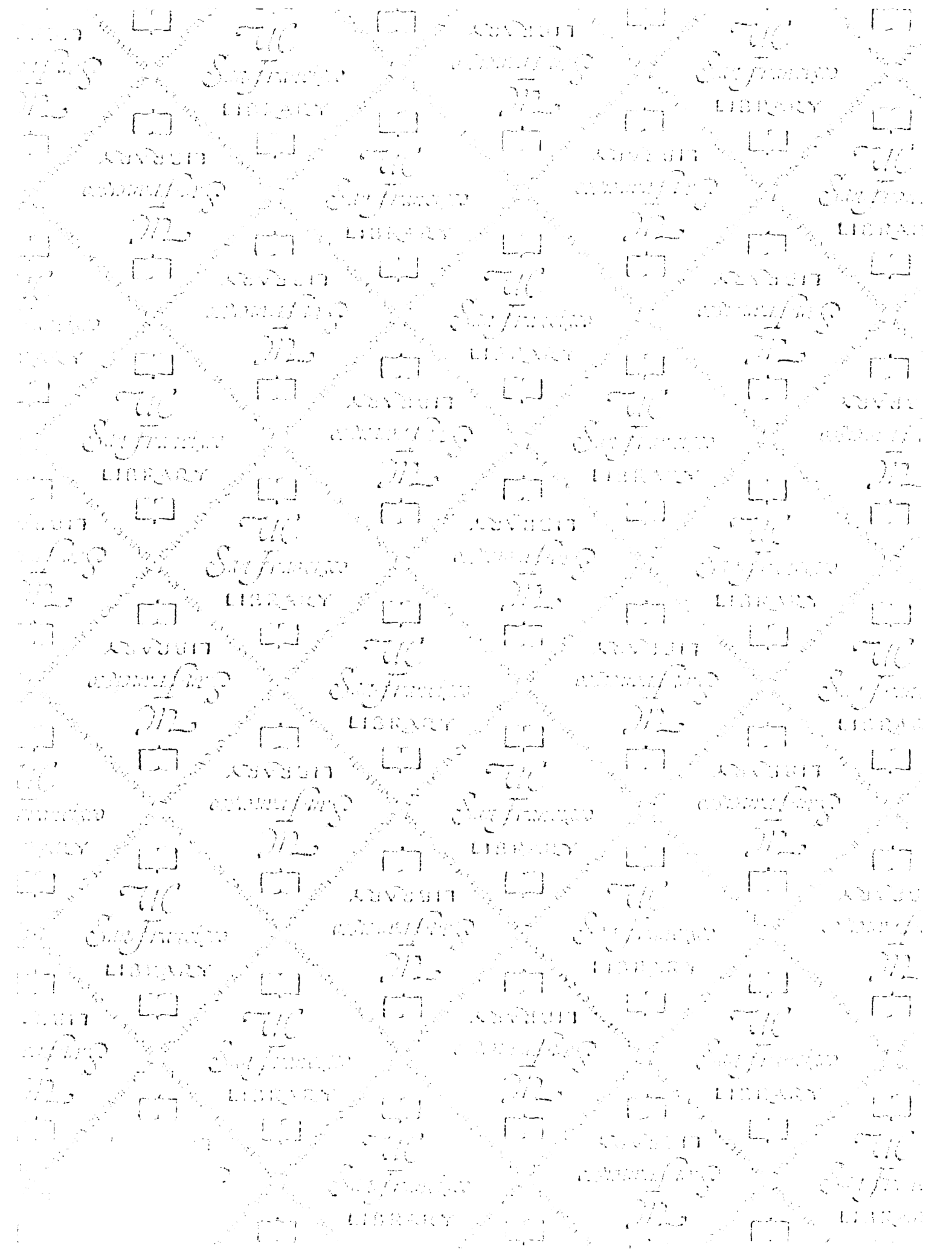VanderWerf, B. A., Kumar, S. S., Pennel, P., & Gotlieb, S. (1978).

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