Arterial Homografts for Peripheral Arteriosclerotic Occlusive Disease

By Michael E. De Bakey, M.D., E. Stanley Crawford, M.D., Oscar Creech, Jr., M.D., and Denton A. Cooley, M.D.

Sympathectomy and thromboendarterectomy have been largely unsatisfactory in the treatment of patients with arterial insufficiency of the lower extremities. In this paper the results are analyzed of a large experience with the use of lyophilized arterial homografts to bridge occlusive lesions below the aortic bifurcation. The criteria for selection of patients for operation, the simplified procedure of end-to-side by-pass of the obstruction, and the excellent results in 145 operations are presented.

Until recently the surgical approach to chronic arterial insufficiency of the lower extremities has been an indirect attack in the form of lumbar sympathectomy. The rationale of this procedure lies in its release of vasoconstrictor tonus and the consequent production of the maximum degree of vasodilatation in the remaining unobstructed arterial bed. It thus produces an increase in the volume of the local vascular bed and consequent improvement in the local circulation. To be sure, this change occurs primarily in the skin and not in the muscular components of the denervated part, but this is a desirable objective, since deficiency in cutaneous circulation of the feet and toes constitutes a major threat to patients with arteriosclerotic peripheral vascular disease. Gangrenous changes take place first in the skin of these parts, not in the muscle; this occurrence, rather than intermittent claudication, is the most common cause for amputation. Accordingly, improvement in blood flow through the skin with the production of dry warm feet assumes major importance.

While there can be little doubt of the benefits that may be derived from sympathectomy in chronic arterial insufficiency of the lower extremities, its limitations must also be recognized. For one thing it is an indirect attack upon the problem; it is not directed toward either the cause of the disease or the organic pathologic changes that have resulted from it. It is merely aimed at improvement in local circulation by producing vasodilatation in those vessels of the part, mainly the collateral vessels, that are still functionally active. For another, it is unlikely to provide significant improvement in intermittent claudication, and patients with this complaint generally persist in having considerable disability. Since sympathectomy has no effect on vessels that have already undergone obliterative structural changes and since this occlusive process usually involves the main arterial channel, it obviously cannot produce adequate restoration of circulation to relieve symptoms under these circumstances and particularly when these changes are associated with a poor collateral vascular bed.

In light of these limitations of sympathectomy and the disappointing results that often follow its use in arteriosclerotic occlusive disease of the lower extremities, efforts have been directed recently toward a better understanding of the disease. This insight had led to the development of a more direct attack upon the occlusive lesion, aimed at restoration of blood flow through the main arterial channel. This much more effective approach to the problem derives from certain pathologic and arteriographic studies by a number of observers. They have shown that the obstructing lesion in chronic arteriosclerotic occlusive
disease of the lower extremities is frequently segmental in nature with a good sized patent segment both above and below the occlusion.6-7 As recognized by Leriche6 many years ago, this fortunate pathologic feature of the disease permits direct attack upon the occlusive process in reestablishing immediate arterial continuity. This possibility became a reality with the development of thrombo-endarterectomy by dos Santos8 and others.9 Unfortunately, the results from endarterectomy have been variable and inconsistent and the reported incidence of failures has been high.10 In our experience postoperative thrombosis has occurred frequently and on at least 4 occasions there was sufficient interference with the existing circulation to cause ischemic changes necessitating amputation.

Bridging such defects by means of blood vessel grafts has proved more consistently successful, and the resultant improvement in circulation has been many times greater than that following sympathectomy.11-15 Accordingly, this communication is concerned with an analysis of our experience with the use of lyophilized arterial homografts in the treatment of 145 extremities with occlusive lesions located below the aortic bifurcation.

**Method and Material**

Arteriography at the appropriate level is performed on all patients entering the hospital with any manifestation of arterial insufficiency of the lower extremity. Those with a patent segment of reasonable size below the obstruction and above the bifurcation of the popliteal artery are selected for operation irrespective of the length of the occlusive process above this level (fig. 1A). In the absence of such a patent segment, as demonstrated on the arteriogram, the graft procedure is not considered feasible and under these circumstances sympathectomy is indicated (fig. 1B). Secondary obstruction in the calf does not alter the results significantly, and, therefore, does not contraindicate operation. The essential requirement is the presence of a good outflow in the peripheral arterial bed as evidenced by palpability of one or more of the distal branches of the popliteal artery. The presence of feebly palpable pulses does not always mean that there is no obstruction, because in several instances palpable pedal pulses have been elicited in patients with either iliac or femoral occlusion. In most of these patients, however, the pulse distal to the occlusion has been significantly weaker than that on the unobstructed side.

Practically all patients with iliac occlusion surveyed in this manner have been candidates for operation. Among the patients with femoral occlusion, however, the incidence of operability was somewhat less and has varied with the clinical manifestations of arterial insufficiency. In those, for example, in whom intermittent claudication was the only indication of inadequate circulation, an operable distal segment has been found in about 75 per cent of the cases, while in patients with inadequate circulation at rest, the incidence of operability has been approximately 55 per cent. It would appear, therefore, that patients with high obstructive lesions involving the iliac arteries near the aortic bifurcation are more likely to have a well localized atherosclerotic occlusive process with a good peripheral arterial bed, whereas those with peripheral lesions tend to have more diffuse arteriosclerotic occlusive disease.

Operability in the diabetic patient is not appreciably different from that in the nondiabetic individual; when the same criteria of selection are applied to these patients, the degree of operative...
success has been the same. Eight patients with Buerger's disease have been surveyed by arteriography and none has proved to be a candidate for operation.

Most patients found to be candidates for operation have had grafts inserted. The few patients with operable lesions not subjected to operation had advanced cardiac or renal disease and the associated intermittent claudication was not considered sufficient indication to justify the risk of surgical intervention. On the other hand, when loss of limb was probable, the risks of the graft procedure were usually accepted inasmuch as this operation was considered a substitute for amputation. In our experience, patients have tolerated peripheral grafting procedures considerably better than either sympathectomy or amputation. This difference is undoubtedly due to the reduction in trauma and the use of immediate ambulation of these older patients with generalized arteriosclerosis.

The indication for operation in most of these patients has been intermittent claudication, which was frequently disabling. Fifteen patients had gangrene of limited degree, and 1 had extensive gangrene. Five patients had painful ischemic ulcers, 29 had severe rest pain, and in 1 a digit had been destroyed by associated infection. Operation was advised in the patient with extensive gangrene to permit a low leg amputation, since the opposite leg had been amputated previously at a higher level.

Table 1.—Results in 145 Operations in which Homografts Were Employed to Replace or By-Pass Arteriosclerotic Occlusive Lesions of the Lower Extremity

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Location of occlusion</th>
<th>Number of operations</th>
<th>Patent grafts Number</th>
<th>Patent grafts Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excision and graft</td>
<td>Iliac</td>
<td>18</td>
<td>17</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>femoral</td>
<td>12</td>
<td>9</td>
<td>75</td>
</tr>
<tr>
<td>End-to-side by-pass</td>
<td>Iliac</td>
<td>61</td>
<td>57</td>
<td>93</td>
</tr>
<tr>
<td></td>
<td>femoral</td>
<td>54</td>
<td>47</td>
<td>87</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>145</td>
<td>130</td>
<td>90</td>
</tr>
</tbody>
</table>

Fig. 2. A. Photograph of an aortogram showing an occlusion of the left common iliac artery. B. Photograph at operation showing the graft in place after excision of the occluded iliac segment.
Technic of Operation

While the primary objective of operations is to restore a normal pulsatile blood flow into the peripheral arterial bed, it should also be the purpose of the operation to minimize recurrence of the disease and to prevent reduction in the existing circulation in the event of graft failure. It is essential, therefore, to bridge the entire occluded segment including all areas of proximal or distal narrowing of the artery; no patent channel, either in the diseased arterial segment or in any collateral vessel, should be sacrificed. Accordingly, the short discrete occlusive segment may be completely excised and replaced by a graft, but longer occlusive segments or those with stenosis or narrowing above or below the area of complete obstruction are preferably treated by the by-pass operation. In our series, for example, there were 30 extremities in which the occlusive lesions were less than 15 cm. in length and all of these were completely excised and replaced by arterial homografts (fig. 2). In the other 115 cases the occlusive areas were longer, multiple, or inconveniently located for excision, so that the by-pass procedure was employed as originally proposed by Kunlin. This by-pass is accomplished by performing an end-to-side anastomosis between the graft and the host artery both above and below the site of occlusion (fig. 3). Usually, 2 small incisions are made that are connected by a tunnel through which the graft extends from one anastomosis to the other (fig. 4). The technical details of the by-pass procedure have been presented elsewhere.

RESULTS

Successful restoration of blood flow distal to the site of occlusion following operation was determined by arteriography or by the presence of palpable pulses below the level of occlusion not felt before operation. Of the 145 extremities treated, a distal pulsatile blood flow was successfully re-established in 130 (90 per cent) (table 1). The failures followed excision and grafting in 4 patients, 1 of whom had an iliac occlusion and 3 femoral artery occlusions. The by-pass procedure failed in 11 patients, 4 of 61 iliac artery and 7 of 54 femoral artery occlusions. These 11 failures were associated with complete distal femoral arterial occlusions in the 4 iliac artery failures; in the 7 femoral occlusions in which the graft did not remain open, the distal patent segment was small and its outflow was so reduced that thrombosis occurred during or soon after operation. The possibility of failure in these
cases was anticipated but operation was attempted in the hope that some increase in blood flow could be obtained. These cases must now be regarded as errors in selection. The arterial circulation in 2 of the 3 femoral arterial excisions and graft failures was made worse by the operation and amputation was subsequently necessary in both these extremities. Particularly significant is the fact, however, that none of these patients who had the by-pass procedure was made worse by the operation.

There was striking improvement in peripheral circulation in those extremities in which the grafts remained patent. Intermittent claudication, rest pain, and pain from ischemic ulceration were immediately and completely relieved in all patients. The ischemic ulcers healed rapidly and the mild gangrenous changes quickly disappeared. The gangrenous infected toe was amputated and the open stump quickly healed. In the patient with extensive gangrene of the foot associated with ischemic changes extending into the thigh, a low leg amputation stump successfully healed following a by-pass graft that re-established a pulsatile circulation down to the ankle. In view of the previous mid-thigh amputation of the other leg, the additional length of this stump afforded by the graft has been of distinct advantage in the rehabilitation of the patient.

Even though most of these operations were done during the past 18 months, a considerable number was performed as long as 2 1/2 years ago. All patients have been carefully followed since discharge and only 2 have had recurrence of symptoms, which in both instances was associated with thrombosis of the graft. One patient had had bilateral intermittent claudication associated with occlusions of the aorta, both iliac and right superficial femoral arteries. The aorta and left common iliac artery were replaced by a homograft and the right iliac and femoral occlusions were by-passed with a homograft extending from the aortic homograft to the popliteal artery. This patient was completely relieved of symptoms after operation and strong pulses appeared throughout both extremities. After discharge from the hospital the patient returned to work and was asymptomatic for 14 months, at which time intermittent claudication returned in the right
leg. This change was associated with the loss of pulses throughout the extremity and a reduction in circulation only equal to that found before operation. The second patient had had a right femoral by-pass graft inserted because of intermittent claudication, severe rest pain, and early gangrenous changes of the toes, which ordinarily constitute adequate indication for low thigh amputation. After operation, pedal pulses were restored with immediate relief of symptoms and rapid regression of the skin changes. This improvement continued until intermittent claudication returned 11 months later. The pulses, which were previously present, could no longer be palpated, but there were no gangrenous changes or rest pain. The distal circulation at this time was considerably better than prior to operation, and regardless of late occlusion of the graft in this case, the emergency period in the circulation of this extremity had been relieved.

Complications

There were 2 deaths in this series due to acute myocardial infarction occurring during operation. One of these patients had an iliac occlusion associated with a large leaking abdominal aneurysm that required emergency operation. The iliac occlusion was treated by insertion of a homograft end-to-side from the common femoral artery to the bifurcation aortic homograft. Had this patient not had rupture of the aneurysm, he would not have been selected for operation in view of his known heart disease. In the other patient who died of coronary occlusion, the complication developed during a second operation performed to control bleeding from a suture line where 2 short homografts had been united to form a long one. This patient probably would have survived and would have been completely rehabilitated had this initial complication not occurred.

A superficial wound infection developed in 1 patient and another had thrombophlebitis associated with a small pulmonary infarct, but both recovered completely without residual disturbances. The single major amputation performed following a by-pass graft was for a part that was destroyed prior to hospital admission. The preoperative circulation was unaltered in the 11 by-pass failures. In the group having excision and graft the circulation of 2 extremities was severely impaired by an unsuccessful operation so that amputation was later required.

Discussion

The results obtained in these patients have been extremely gratifying. In our experience these results are far superior to other operations, particularly lumbar sympathectomy. It has been a rewarding experience to observe gangrenous changes regress almost overnight and older patients with severe disabling symptoms resume their normal activities. The few poor results were due to errors in selection of patients for operation.

On the basis of this experience several factors assume major importance in contributing to the gratifying results obtained from this method of therapy. These include particularly the proper selection of cases, the use of freeze-dried arterial homografts, and, perhaps above all, employment of the simplified technic of the end-to-side by-pass procedure.

As emphasized previously, there are 2 important considerations in the selection of patients for operation. The first is concerned with the risk to life and limb. Obviously in the patient with severe impairment of cardiac or other vital function who has only intermittent claudication, operation may be contraindicated not only because of the increased risk, but also because under these circumstances the patient's activities will not be altered by improvement in circulation of the extremities. On the other hand, in patients with occlusive lesions that threaten loss of the extremity, operation may be indicated on the basis that they can withstand the grafting procedure, which might preserve the extremity, as easily as, if not more easily than, an amputation.

The second consideration in the proper selection of patients for operation is concerned with the presence of an adequate patent peripheral arterial bed below the occluded segment for the ready outflow of blood. This can be readily established by proper arteriographic
The availability of arterial homografts, preserved by the freeze-drying process, has undoubtedly contributed significantly to the successful application of this method of therapy. The advantages of this type of blood vessel graft are numerous, including particularly ease and simplicity of preparation, assurance of general uniformity of caliber, and facility in technical performance of anastomosis.

The end-to-side by-pass operation is undoubtedly a highly important, if not the most important, factor that has contributed to the success of direct surgical attack in these cases. It is based upon the natural response of the arterial bed to occlusion, that is, development of collateral vessels around the obstructed area. Thus, the operation consists essentially in the addition of an artificial collateral artery around the obstruction, which, being as large as the host vessel, assures immediate maximum restoration of a distal pulsatile blood flow.

The technical features of the operation, like its conception, are simple. The small incisions require minimal dissection; thereby injury to adjacent structures is reduced. The host artery is only slightly disturbed and no collateral branch is sacrificed (fig. 5). The most normal section of host artery both above and below the occlusion can be selected for anastomosis, irrespective of the intervening distance and without fear of jeopardizing existing collateral circulation or increasing significantly the extent of operation. If the procedure fails to restore normal circulation, or if the graft becomes occluded later, it does not alter the circulation already present in the leg. In addition to these technical advantages, a high degree of success has been obtained without significant complications and with minimal risk to life and limb.

In the early phase of this study, it was thought that relatively short occlusive segments might be best treated by excision and graft replacement. As experience was gained with the by-pass procedure, however, and its distinct advantages in simplicity of performance and in providing a high degree of success with minimal risk became more apparent, it has become the procedure of choice in our hands even in cases with relatively short occlusive lesions.

This experience has also led us to abandon
the use of lumbar sympathectomy as a supplemental procedure as was done routinely in our earlier cases. It is now employed only in cases in which the occlusive process is not associated with a patent distal segment (fig. 1B). Of particular interest is the fact that lumbar sympathectomy had been previously performed on 19 of the patients in this series, none of whom obtained adequate relief of symptoms. Following the grafting procedure all were completely relieved of their manifestations of arterial insufficiency.

Finally, and of particular importance, is the impressive fact that this form of therapy is applicable in the majority of patients with arteriosclerotic arterial insufficiency of the lower extremities, which is by far the most common type of peripheral vascular disease. This wide applicability is well illustrated by observations derived from our experience with this method of study during the past several years. Thus among all cases examined and found on arteriography to have iliac occlusion, virtually all proved to be candidates for operation and successful results were achieved in 93 per cent of these cases. Although this incidence of operability was somewhat less among patients with femoral occlusions, it is noteworthy that well over one half of them were found to be candidates for operation and successful results followed operation in 87 per cent of the cases. It is thus apparent that this form of management not only provides a high degree of success but also may be employed in the majority of patients with arterial insufficiency of the lower extremities.

Summary

Results of indirect methods of treating peripheral arterial insufficiency of the lower extremities have been generally disappointing. The response in any 1 case has been difficult to predict. Rest pain and intermittent claudication are relieved infrequently. Sympathectomy has offered little or no absolute certainty against amputation for many of the manifestations of arterial insufficiency.

Arteriographic studies on patients with chronic arterial insufficiency of the lower extremities have demonstrated that the occlusive lesion is localized and discrete with a patent vessel above and below it in the majority of instances. As a consequence of this pathologic feature of the disease, it is possible to restore distal circulation immediately in most of these patients by direct surgical means and thus assure immediate relief of symptoms, healing of cutaneous lesions, and prevention of amputation. Several methods of direct attack have been devised, the most consistently successful of which has consisted in substitution of an arterial homograft for the obstructed segment.

This procedure may be accomplished by either of 2 technics. The occlusion may be completely excised and replaced by a graft, or a graft can be used to by-pass the occlusion by suturing the graft end-to-side both above and below the occlusion. In the early phases of this study the former method was used in short discrete lesions and the latter for longer occlusive segments. More recently, and because the end-to-side by-pass procedure has proved superior, it has been employed almost exclusively.

These procedures were employed in 145 extremities for occlusion, 79 of which involved the iliac and 66 the femoral artery. Excision and grafting were performed in 30 extremities, 18 with iliac and 12 femoral arterial occlusion. The by-pass procedure was used in 115 extremities, 61 of which had iliac and 54 femoral arterial occlusion. A pulsatile blood flow distal to the occlusion was successfully restored and all symptoms were relieved in 90 per cent of the cases. Approximately 15 to 20 per cent of these patients were candidates for immediate or early amputation. This procedure was prevented in all but 1 patient whose foot had already been destroyed prior to operation.

There were 2 hospital deaths from coronary thrombosis, and 2 low thigh amputations were required following failure of excision and grafting. The circulation was not affected in any of the 11 patients in whom the by-pass operation was unsuccessful.

Summario in Interligna

Le risultati de indirecte methodes de tractamento de peripheric insuffictencia arterial del
extremidades inferior es generalmente desappuntante. Le responsas in le specific caso individual es difficile a predicir. Dolor de reposo e claudication intermittente es alleviate infrequentemente. Sympathectomia ofere pauc o nulle absolute certitude del obviation de amputation pro multes del manifestationes de insufficientia arterial.

Studios arteriographic de patientes con chronic insufficientia arterial del extremidades inferior ha demonstrate que le lesion obliterante es localisate e discrete con un vaso patente supra e infra su sito in le majoritate del casos. Como consequencia de iste caracteristica pathologic del morbo, il es possibile restaurar le circulation distal immediamentemente in le majoritate de iste patientes per directe medios chirurgic, con consequente assecurantia del immediate alleviamento del symptomas, de curation de lesions cutanee, e del obviation de amputationes. Varie metodos de attacco directe ha essite disvolveppate. Inter illos le plus uniformemente succedente ha consistite in le insertion de un homografo arterial in loco del segmento obstruite.

Iste manovra pot esser executate in un de duo manieras. Le occlusion pot esse complemente excidite e reimplaciate per un graffo, o le graffo pot esser usate in contornar le occlusion per suturar lo termino-a-parieta supra e infra le occlusion. Durante le prime phases del presente studio le methodo a excision complete essite usate in curte lesions discrete, e le methodo a derivation essite usate in casos de occlusion de plus longe segmentos. Plus recentemente, le methodo a suturation termino-a-parieta se ha provate superior e ha essite usate quasi exclusivamente.

Iste manovras essite emplate in 145 extremitates con occlusion arterial. In 79 casos le arteria iliaca essite implicate; in 66 casos il se tractava del arteria femoral. Excision e graffo essite emplate in 30 extremitates, 18 con occlusion del arteria iliaca, 12 con occlusion del arteria femoral. Le methodo a derivation essite emplate in 115 extremitates, 61 con occlusion del arteria iliaca, 54 con occlusion del arteria femoral. Un fluxo pulsatile de sanguine distal al occlusion essite restaurate con bon successo e omne le symptomas essite alleviate in 90 pro cento del casos. Circa 15 a 20 pro cento de iste patientes esseva candidatos pro immediate o imminente amputationes. Le amputationes esseva evitate in omne casos, con un exception. In isto, le pede esseva jam destruite ante le operation.

Occurreva in le serie 2 mortes hospitalari ab thrombosis coronari. Duo amputationes infero-femoral esseva requirete post non-successo de excision con graffo. Le circulation non esseva afficite in ulle del 11 patientes in qui le operation a derivation non succedeva.

REFERENCES


Hypertension is defined by its negative characteristics and is identified by exclusion. It represents a group of individuals with elevated blood pressure without a discoverable causal lesion. Because of the practice of differentiating normal blood pressure from elevated blood pressure, the concept has developed that essential hypertension is a specific pathologic entity with a single and unitary cause. Hypotheses in regard to the nature of its cause are numerous. Examination of the evidence on which the current concepts are based demonstrates that this concept is not justified. In the general population, distribution curves of the frequency of blood pressure demonstrate a continuous variation. The observed facts do not justify the differentiation of the population on the basis of the blood pressure. If there exists a group in which the blood pressure does not increase with advancement in age, it would seem that this represents a very small group, and to designate such individuals as having normal blood pressure would seem to be a wrong terminology. It has frequently been proved that the malignant phase follows as a direct consequence of the intensity of the hypertension and of the rapidity with which the blood pressure rises. The malignant phase can be reverted to the benign phase by various medical therapeutic procedures. Also, the differentiation between normal blood pressure and the benign and malignant phases of high blood pressure is fundamentally of a quantitative rather than a qualitative character. The malignant phase of hypertension forms a compact clinical group because it reflects a well-defined vascular lesion, acute fibrinoid arteriolar necrosis, with a relatively well-defined cause. By contrast, the benign phase is extremely heterogeneous and merges imperceptibly into the population at large. This is true because the chief vascular abnormalities of the benign phase are found also in those subjects with lower pressures though they are probably less frequent and less severe and carry a smaller hazard. The chief risk, heart failure, is probably, at least in part, a consequence of the height of the arterial pressure, for there is now little doubt that if an initially grossly raised arterial pressure is lowered by sympathectomy or hypertensive drugs, the heart failure may resolve. The arterial lesions of the benign phase more specifically associated with hypertension, i.e., elastosis and fatty hyaline thickening of arterioles, have not been produced experimentally but may represent the effects of high blood pressure; their clinical consequences would, however, seem relatively unimportant. Arterial disease and high blood pressure are phenomena of different orders and should not be confused. It is the height of the blood pressure that matters. It is not intended to imply that arterial disease is unimportant. Arterial disease is, in most of us, of much greater moment than the height of the arterial pressure, but its study presents a peculiar difficulty, i.e., that of determining its presence, extent, and type prior to the occurrence of vascular catastrophe or the death of the patient. The important arterial lesions in the benign phase of hypertension also occur in patients with lower blood pressure though perhaps less frequently and less severely. The intensity of the hypertension is clearly a factor in the production of hypertensive heart failure. The phenomena of the malignant phase are consequences of an extremely severe hypertension. A study of the clinical features of essential hypertension supports the idea that blood pressure behaves as a graded characteristic, increasing the severity or the risk of certain disorders of large arteries, increasing the load on the heart and when it exceeds a certain threshold, precipitating acute fibrinoid arteriolar necrosis, which is the basis of the malignant phase.
Arterial Homografts for Peripheral Arteriosclerotic Occlusive Disease
MICHAEL E. DE BAKEY, E. STANLEY CRAWFORD, OSCAR CREECH, JR.
and DENTON A. COOLEY

Circulation. 1957;15:21-30
doi: 10.1161/01.CIR.15.1.21
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1957 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/15/1/21

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/