PAPERS AND ORIGINALS

Comparison between Sequelae of Surgical and Medical Treatment of Venous Thromboembolism

A. E. YOUNG, M. LEA THOMAS, N. L. BROWSE

British Medical Journal, 1974, 4, 127-130

Summary

Thirty-six patients have been studied clinically and phlebographically three years after a major deep vein thrombosis. Twenty were treated surgically and 16 medically. The incidence of post-thrombotic symptoms was similar in the two groups. The use of superficial femoral vein ligation to prevent embolism will not worsen the prognosis of a leg which is already the site of deep vein thrombosis.

Introduction

There are doubts about the value of the surgical treatment of venous thrombosis in the absence of a need to protect against pulmonary embolism. But it has been our clinical impression that the addition of a surgical procedure to prevent embolism does not increase the prospects of post-thrombotic symptoms developing in a leg that is already the site of venous thrombosis. Consequently, we have repeatedly emphasized the importance of the rapid and thorough investigation of patients with pulmonary embolism with every available technique and proposed an aggressive but planned, logical approach to treatment, which includes surgery when deemed necessary. This has reduced the incidence of recurrent pulmonary embolism in the first month of treatment from 24% to 2% (Browse *et al.*, 1969). The plan of management is tripartite.

Firstly, prompt and adequate anticoagulation is begun with heparin on the basis of the clinical diagnosis unless there are very strong contraindications. This can be continued and replaced by oral anticoagulants after the diagnosis has been confirmed by phlebography and treatment planned.

Secondly, precise information about the nature and extent of the thrombosis is obtained urgently by phlebography (Thomas, 1972). Ascending phlebography is usually sufficient but needs to be supplemented by percutaneous femoral or pertrochanteric intraosseous injections in 7% of cases (Browse and Thomas, 1974). Both limbs must always be examined.

Thirdly, a thrombus that is judged by its phlebographic appearance to be capable of becoming an embolus is removed or "locked in." Adherent thrombi are left alone and further thrombosis is prevented with anticoagulants. The phlebographic appearance of a thrombus as it ages has been described elsewhere (Thomas and McAllister, 1971).

Many clinicians are content to treat all venous thromboembolism solely with anticoagulants, even when phlebography shows loose thrombi. They support this attitude by claiming that surgery, especially vein ligation, may cause severe venous insufficiency in the legs and produce the post-thrombotic syndrome (pain, swelling, pigmentation, eczema, and ulceration). Our experience disagrees with this view, and the object of this study was to compare two groups of patients with thrombi of comparable extent, one treated with anticoagulants and the other with surgery and anticoagulants, to see if the addition of vein ligation to prevent embolism did harm to the leg. This was not a controlled, randomly allocated clinical trial because we believed in the light of our previous studies that it was unethical to withhold surgical treatment from patients with loose thrombi.

Methods

Of the 250 patients who presented with pulmonary embolism between 1965 and 1972 73 had a loose thrombus, which we considered should be removed or "locked in." After excluding those with a previous history of venous thrombosis and varicose veins we were left with 20 patients who were prepared to come for a clinical examination and phlebography. These constituted the surgical group. Sixteen patients were picked out of our files at random from the same period with phlebograms that showed thrombi of similar extent but who were not treated surgically because the upper end of the thrombus was fixed. These patients were also reviewed and underwent x-ray examination, and they made up the medical group.

St. Thomas's Hospital, London S.E.1

A. E. YOUNG, M.B., F.R.C.S., Surgical Registrar

M. LEA THOMAS, M.R.C.P., F.F.R., Consultant Radiologist

N. L. BROWSE, M.D., F.R.C.S., Professor of Vascular Surgery

TABLE I—Extent of Thrombosis discovered at Initial Phlebography in Two Groups of Patients

	No. of Patients	No. with Bilateral Thrombosis	No. with Unilateral Thrombosis	Total No. of Thrombosed Legs	Highest Extension of Clot		
					Popliteal Vein	Superficial Vein	Iliac/Common Femoral Vein
Medical group	16	3	13	19	6	9	4
Surgical group	20	6	14	26	11	7	8

TABLE II—Comparison Between Two Groups of Patients Studied

	No. of Patients	Sex		(Age Years)		Origin of Thrombosis			No. (%) with Pulmonary Embolus	Mean (Range) Duration of Follow up (Months)		Mean Duration of Anticoagulant Treatment* (Months)
		M.	F.	Mean	Range	Post-operative	Medical Illness	Spontaneous		Clinical	Phlebographic	
Medical group	16	10	6	57	25-72	2	1	13	9 (56)	39.5 (12-75)	23 (12-50)	4
Surgical group	20	14	6	57	20-72	7	2	11	12 (60)	34.5 (17-79)	27 (13-48)	4

*Two patients in each group did not receive anticoagulants.

The development of varicose veins and the presence of pain or discomfort in the legs on walking or standing, itching, eczema, and ulceration were recorded and the follow-up phlebograms examined to assess the degree of recanalization, the presence and site of collateral veins, the presence of valves in recanalized segments, and the presence of incompetent perforating veins.

INITIAL THROMBOSIS

A thrombus was present in 26 legs of the 20 patients in the surgically treated group and in 19 of the medical group. The highest segment involved is shown in table I. In only one case was an iliofemoral or superficial femoral vein thrombosis not continuous with calf thrombosis.

Seven patients in the surgical group had bilateral superficial femoral vein ligations though the phlebogram showed thrombus in only one leg. This was done because we were not certain in the early years how accurate phlebography was. As a complete superficial femoral vein thrombosis occurred immediately distal to the site of ligation in these seven legs they are identical to and counted as "thrombosed legs" in the follow-up figures, making 33 thrombosed legs in the surgical group and 19 in the medical group.

INITIAL TREATMENT

Anticoagulants were contraindicated in two patients in each group. All the other patients in both groups were given anticoagulants—for three to five days with heparin and then with oral agents. None were on anticoagulants for less than a month. The mean duration of anticoagulation was four months in both groups.

The type of surgery performed was determined by the extent of the thrombosis seen on the phlebogram. Two patients had inferior vena cava ligation (one ligation affected two legs), 21 had superficial femoral vein ligation alone (including the seven prophylactic ligations), seven had superficial femoral vein ligation and proximal thrombectomy, and three had thrombectomy alone. There were no deaths or serious complications attributable to surgery.

Results

The two groups were comparable in terms of age, sex, duration of follow up, and anticoagulation (table II).

The clinical follow-up findings in each group are detailed in table III. Because the samples were small apparent differences

TABLE III—Findings at Clinical Follow Up

	No. (%) of Thrombosed Legs		No. (%) of Legs Without Thrombosis (20 Legs)
	Surgical Group (33 Legs)	Medical Group (19 Legs)	
New varicose veins ..	11 (33)	2 (11)	5 (25)
Swelling ..	21 (64)	11 (58)	7 (35)
Pain or discomfort ..	17 (52)	12 (63)	5 (25)
Pigmentation ..	6 (18)	3 (16)	2 (10)
Ulceration ..	3 (9)	3 (16)	0
Postphlebotic syndrome*	15 (45)	11 (58)	4 (20)
Symptom Free ..	5 (15)	4 (21)	8 (40)

*A diagnosis of postphlebotic syndrome was made when at least two symptoms, not including varicose veins, were present.

between some groups were not statistically significant (χ^2 test, two tailed). If the results are assessed by calculating a symptom score on the basis of one point per symptom there was no significant difference between the medical and surgical groups and no difference between the effects of vein ligation performed when thrombus was present in the leg before operation and ligation in the absence of phlebographically demonstrable thrombus (table IV).

TABLE IV—Symptom Scores for Legs on Clinical Follow Up

	Thrombosed Legs			Normal Legs
	Medical Group	Surgical Group		
		Thrombosed before Operation	Prophylactic Superficial Femoral Vein Ligation	
No. of legs	19	26	7	20
Score	32	45	12	17
No. of symptoms per leg	1.68	1.73	1.71	0.85

Altogether 45% of the surgical group and 32% of the medical group were wearing elastic stockings and the complaint of itching was confined to these patients. It was impossible to exclude a causal relationship between the two and so itching was excluded from symptom comparisons between the groups.

The phlebograms showed that recanalization of the popliteal vein and the iliac segment was common in both groups (table V). Complete recanalization of the superficial femoral vein was uncommon, and this segment was usually bypassed by large collaterals passing to the profunda femoris vein or by enlarged venae comitantes. In no case did the collateral channels look large enough to allow the passage of a large embolus.

When phlebography is performed to show the state of the deep veins it does not always show the competence of the perforating veins. Incompetent perforating veins were seen in about

TABLE V—Results of Follow up Phlebography

	Surgical Group		Medical Group	
	% of Legs	No. of Legs Available for Study	% of Legs	No. of Legs Available for Study
Iliac Segment:				
Recanalization	100	8	100	4
Collaterals	0	8	0	4
Superficial Femoral Vein:				
Recanalization	3	29	14	14
Bypassed by profunda femoris..	76	29	57	14
Bypassed by venae comitantes..	35	29	79	14
Popliteal Vein:				
Recanalization	88	25	79	19
Collaterals	12	25	21	19

one-third of the legs in each group, but this is probably an underestimate of the number actually present. There was no difference between the groups.

A new episode of thrombosis occurred between the time of the original phlebogram and the follow up in the legs of two patients, one in each group. As the effects of this new thrombosis were not directly attributable to the initial treatment the legs involved are not included in table V.

Discussion

The syndrome of swelling and pain in the legs leading to eczema, pigmentation, varices, induration, and eventually ulceration has long been known to be a sequel of venous thrombosis. Thirty years ago Bauer showed that 80% of patients attending with these symptoms gave a history of venous thrombosis in the legs, and he showed a correlation between these physical signs and phlebographic evidence of deep vein insufficiency (Bauer, 1942). Those patients who do not give a definite history of thrombosis may nonetheless have suffered a no less extensive but asymptomatic thrombosis (Sevitt and Gallagher, 1961).

It is recognized that though the interval between the thrombosis and the development of post-thrombotic symptoms may be as long as 10 or 20 years the symptoms usually begin much earlier. Twenty of the 21 patients with venous thrombosis followed up by Phillips (1963) had some symptoms of venous insufficiency within 30 months. Thus a follow up at three years is likely to give a reasonable estimate of the likelihood of late complications.

The object of the treatment of venous thrombosis is three-fold: the relief of the presenting symptoms, the prevention of pulmonary embolism, and the prevention of the development of the post-thrombotic syndrome. Most important is the prevention of pulmonary embolism and treatment must primarily be directed

to this end even if it does nothing to help or even worsens the prospect of post-thrombotic leg symptoms.

Current methods for the treatment of established thrombosis fall into five main groups: conservative measures such as elevation, bandaging, and exercise; anticoagulants; thrombolytic agents; surgical thrombectomy; and venous interruption. None guarantees to produce a leg free of post-thrombotic changes. Simple "conservative" measures are of no value either in the prevention of pulmonary embolism or in the lessening of post-thrombotic changes (Sevitt and Gallagher, 1959; Flanc *et al.*, 1969; Rosengarten *et al.*, 1970). Anticoagulants decrease the mortality of pulmonary embolism (Barritt and Jordan, 1960) and the incidence of embolism after surgery (Sevitt and Gallagher, 1961) but do little to prevent the recurrence of pulmonary embolism after a "herald" embolus (Browse *et al.*, 1969), and anticoagulants do not prevent the late sequelae of thrombosis (Phillips, 1963). Thrombectomy is advocated primarily for the management of iliofemoral thrombosis, but the late results seem to be no better than those obtained with other methods, rethrombosis after thrombectomy being the rule rather than the exception (Karp and Wylie, 1966). Lansing and Davies (1968) reviewed a series of 34 thrombectomies performed at least five years earlier. At an 18-month follow up 83% of the patients had had phlebograms showing nothing abnormal, but at five years phlebograms on 15 of the 25 survivors showed deep venous insufficiency, and only one of the 25 patients was free of post-thrombotic symptoms in the legs. If thrombolytic agents were to leave the valves intact they could be expected to yield the best long-term results, but complete clearance of the thrombosis is not always obtained and the valves are often left incompetent (Browse *et al.*, 1968; Kakkar *et al.*, 1969; Mavor *et al.*, 1973).

The incidence of the post-thrombotic syndrome, as shown in the random selection of published results in table VI, indicates that thrombectomy, anticoagulants, and thrombolytic therapy are all likely to leave a high proportion of obstructed segments and damaged valves just as extensive as after a distal vein ligation though without such effective protection against embolism.

The patients examined in our study were to a considerable extent self-selected in that many suitable for follow up failed to answer questionnaires, attend for examination, or consent to further phlebography. It could be argued that the attenders might contain a large proportion of those with symptoms, their motive for attending being a hope of improvement. As both groups will reflect this sampling error, however, the primary intention of comparing the late results of medical and surgical treatment is not invalidated, but the incidence of post-thrombotic symptoms may be falsely high.

TABLE VI—Late Effects of Various Forms of Management of Venous Thrombosis from 1949-70

Treatment	No. of Patients	Period of Follow up (Years)	Sequelae		
			(%) Symptom Free	Incidence of Post-thrombotic Syndrome (%)	Criteria for Diagnosis of Post-thrombotic Syndrome
Lillie <i>et al.</i> (1949)	10	0.5-?	20	60	Pain and swelling
Agrifoglio and Edwards (1961)	21	5-10	?	10	Ulcers
Mozes (1966)	118	0.25-7	42	13	"Severe" sequelae
Piccone <i>et al.</i> (1970)	22	0.5-18	12.5	69+	Post-thrombotic syndrome
Wheeler <i>et al.</i> (1966)	35	?-12.5	?	66	"Stasis disease"
Bowers and Leb (1955)	25	?-?	34	60	Ulcers
Shea and Robertson (1951)	25	2-7	4	60	Ulcers/trophic changes
De Meester <i>et al.</i> (1967)	35	0.1-6	28	17	Ulcers
Wheeler <i>et al.</i> (1966)	35	?-2.5	?	20	"Stasis disease"
Lillie <i>et al.</i> (1949)	59	0.5-?	23	42	Pain and swelling
Agrifoglio and Edwards (1961)	144	5-10	1	1	Post-thrombotic syndrome
Robinson and Meyer (1954)	12	4-4	0	83	Ulcers
Adams and De Weese (1970)	30	0.2-1	53	2	Post-thrombotic syndrome
Lillie <i>et al.</i> (1949)	30	0.5-?	32	38	Pain and swelling
Agrifoglio and Edwards (1961)	21	5-10	90	0	Dermatitis and oedema
Robinson and Meyer (1954)	32	5-5	81	5	Post-thrombotic syndrome
Adams and De Weese (1970)	39	0.3-6	25	54	Post-thrombotic syndrome
Szilagyi and Alsop (1949)	100	0.1-7	33	27	"Moderate" sequelae
Lillie <i>et al.</i> (1949)	81	0.5-?	41	46	Pain and swelling
Fuller <i>et al.</i> (1960)	416	?-?	?	6.5	Post-thrombotic syndrome
Phillips (1963)	22	2-3	45	4.5	Pigmentation and eczema
Mavor and Galloway (1969)	83	0.2-7	54	9	"Venous insufficiency"
Lansing and Davis (1968)	25	5-5	4	4	Ulcers

The clinical findings show that apart from the development of new varicose veins there was no significant difference in the incidence of fully developed or incipient post-thrombotic syndrome, as judged by the presence of pain, swelling, pigmentation, and ulceration, between the legs of patients treated solely with anticoagulants and the legs of those treated surgically. The prophylactic vein ligations gave an incidence of post-thrombotic syndrome similar to that of the thrombosed legs. Thus one may predict that venous surgery performed on a thrombosed leg will not worsen it, but prophylactic vein interruption may produce complications. These results substantially agree with those of Szilagyi and Alsop (1949), who studied a similar series of patients. Their results after surgery were no worse than ours yet most of their patients did not receive anticoagulants. Our 20 patients treated surgically represent approximately the number that would need surgery if 100 patients with embolism were investigated, and the proportion of the different forms of surgery were also typical (Browse *et al.*, 1969). The results are no different if the vena caval ligation and the three thrombectomies are removed.

The cause of the venous insufficiency found in 60% of the legs which had never been shown clinically or phlebographically to be the seat of venous thrombosis is not clear. The tendency for venous thrombosis to be bilateral is well known and it may be that there is a high incidence of undetected minor thrombosis in "normal" legs, but if so it is surprising that such a minor thrombosis can damage the veins to an extent that gives rise to severe postphlebotic symptoms.

The phlebograms show that the state of the deep veins of the leg after treatment with anticoagulants alone is similar to that seen after treatment with surgery and anticoagulants. All the iliac segments and most of the popliteal veins had recanalized but recanalization was rare in the superficial femoral vein, probably because of the pre-existence of a large, normal bypass system between the upper popliteal vein and the profunda femoris vein. The basic similarity between the phlebographic

appearances of the two groups two years after the thrombosis confirms our contention that the addition of a surgical procedure to prevent embolism does not increase the prospect of post-thrombotic symptoms developing in a leg that is already the site of venous thrombosis. The similarity between the groups also raises grave doubts about the value of the surgical treatment of thrombosis in the absence of a need to protect against embolism.

References

- Adams, J. A., and De Weese, J. A. (1970). *Annals of Surgery*, 172, 795.
 Agrifoglio, G., and Edwards, E. A. (1961). *Journal of the American Medical Association*, 178, 1.
 Barritt, D. W., and Jordan, S. C. (1960). *Lancet*, 1, 1309.
 Bauer, G. (1942). *Acta Chirurgica Scandinavica*, 86, Supp. No. 74.
 Bowers, R. F., and Leb, S. M. (1955). *Surgery*, 37, 622.
 Browse, N. L., Thomas, M. L., and Pim, H. P. (1968). *British Medical Journal*, 3, 717.
 Browse, N. L. *et al.* (1969). *British Medical Journal*, 3, 382.
 Browse, N. L., and Thomas, M. L. (1974). *Lancet*, 1, 258.
 De Meester, T. R. *et al.* (1967). *Surgery*, 62, 56.
 Flanc, C., Kakkar, V. V., and Clarke, M. B. (1969). *Lancet*, 1, 477.
 Fuller, C. H., Robertson, C. W., and Smithwick, R. H. (1960). *New England Journal of Medicine*, 263, 983.
 Kakkar, V. V. *et al.* (1969). *British Medical Journal*, 1, 806.
 Karp, R. B., and Wylie, E. J. (1968). *Surgical Forum*, 17, 147.
 Lansing, A. M., and Davis, W. M. (1968). *Annals of Surgery*, 168, 620.
 Lillie, R. H., Buxton, R. W., and Duff, I. F. (1949). *Archives of Surgery*, 59, 609.
 Mavor, G. E. *et al.* (1973). *British Journal of Surgery*, 60, 468.
 Mavor, G. E., and Galloway, J. M. D. (1969). *British Journal of Surgery*, 56, 45.
 Mozes, M. *et al.* (1966). *Surgery*, 60, 790.
 Phillips, R. S. (1963). *Archives of Surgery*, 87, 732.
 Piccone, V. A. *et al.* (1970). *Surgery*, 68, 980.
 Robinson, J. R., and Moyer, C. A. (1954). *Surgery*, 35, 690.
 Rosengarten, D. S. *et al.* (1970). *British Journal of Surgery*, 57, 296.
 Sevvit, S., and Gallagher, N. (1959). *Lancet*, 2, 981.
 Sevvit, S., and Gallagher, N. (1961). *British Journal of Surgery*, 48, 475.
 Shea, P. C., and Robertson, R. L. (1951). *Surgery, Gynecology and Obstetrics*, 93, 153.
 Szilagyi, D. E., and Alsop, J. F. (1949). *Archives of Surgery*, 59, 633.
 Thomas, M. L. (1972). *Archives of Surgery*, 104, 145.
 Thomas, M. L., and McAllister, V. (1971). *Radiology*, 99, 37.
 Wheeler, C. G. *et al.* (1966). *Annals of Surgery*, 163, 199.

Low-dosage Ancrod for Prevention of Thrombotic Complications after Surgery for Fractured Neck of Femur

W. W. BARRIE, E. H. WOOD, P. CRUMLISH, C. D. FORBES, C. R. M. PRENTICE

British Medical Journal, 1974, 4, 130-133

Summary

The effect of a low-dosage regimen of ancrod in the prevention of postoperative deep vein thrombosis was assessed in 24 patients having surgical repair of fractured neck femur and compared with 25 control patients who did not receive therapy. The objective of the therapy was to lower the preoperative fibrinogen level and produce a low concentration of fibrin degradation products

yet avoid the haemorrhagic complications of total defibrination. Ancrod therapy proved feasible to carry out, was not associated with haemorrhagic complications, and produced sustained, predictable reductions in fibrinogen concentration. There were seven thromboembolic complications in the control patients compared to one such complication in the ancrod-treated patients. Five deaths occurred in the control group and one in the treated group. Though the incidence of deep vein thrombosis was not apparently affected by ancrod it appeared on venography that the thrombi in the treated patients were less extensive than those in the control patients. Finally, some discrepancies in the diagnosis of deep vein thrombosis by the three techniques of clinical examination, ¹²⁵I-fibrinogen scanning, and ascending venography were identified.

Introduction

Pulmonary embolism, which is a serious cause of postoperative morbidity and mortality (Coon and Coller, 1959; Sevvit, 1962;

Royal Infirmary, Glasgow G4 0SF

W. W. BARRIE, F.R.C.S., Registrar, Orthopaedic and Accident Division
 E. H. WOOD, F.R.C.S., Senior Registrar, Orthopaedic and Accident Division
 P. CRUMLISH, D.M.R.D., Registrar, Department of Radiology
 C. D. FORBES, M.D., F.R.C.P., Senior Lecturer, University Department of Medicine
 C. R. M. PRENTICE, M.D., M.R.C.P., Wellcome Research Fellow and Honorary Consultant Physician