DEATH AND THROMBOEMBOLIC DISEASE AFTER TOTAL HIP REPLACEMENT

A SERIES OF 1162 CASES WITH NO ROUTINE CHEMICAL PROPHYLAXIS

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We studied 1162 consecutive total hip replacements (THR) to establish the incidence of fatal pulmonary embolism (PE), clinical non-fatal PE and deep-vein thrombosis (DVT) in the six months after surgery. Chemical thromboprophylaxis had not been routinely used. We used a validated questionnaire supplemented by post-mortem records and a review of the clinical notes. Follow-up was 100%.

The death rate from PE was 0.34% (95% CI 0.09 to 0.88), with one fatal PE after discharge 40 days after operation. The clinical PE rate confirmed by imaging was 1.20% (CI 0.65 to 2.02), with 0.7% of patients readmitted. The venographically-confirmed clinical DVT rate was 1.89% (CI 1.11 to 2.76), with 1.13% readmitted. The total thromboembolic morbidity was 3.4% (95% CI 2.5% to 4.7%); prophylaxis to reduce this would be justifiable if the complications of such prophylaxis did not produce an alternative morbidity.

The fatal PE rate after THR without routine chemical prophylaxis was low; a very large randomised clinical trial would be required to demonstrate directly whether any prophylactic measure could reduce this. There is a large discrepancy between the high DVT rate reported in clinical trials using universal screening venography and the symptomatic DVT rate shown in this study. We found insufficient evidence to recommend continuing thromboprophylaxis after discharge from hospital.

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Thromboembolism is one of the most common and potentially serious complications of total hip replacement (THR). Early series suggested that the mortality from pulmonary embolism (PE) could be as high as 2.3% to 3.4% (Coventry, Nolan and Beckenbaugh 1973; Johnson, Green and Charnley 1977) and such historical control figures are still repeated in support of thromboprophylaxis (European Consensus Statement 1991) or a particular prophylactic regimen (Paiement et al 1993). More recent series suggest an overall mortality of 0.95% to 1.1%, with that due to PE only a proportion of this (Sheppard et al 1981; Seagroatt et al 1991). It seems that the death rate from PE may be falling and that updated mortality figures are required.

Venographic studies have shown an incidence of deep-vein thrombosis (DVT) without prophylaxis of about 45%, but only a small proportion of these thrombi present clinically as DVT or PE. Similarly, screening ventilation-perfusion (V/Q) studies have shown an incidence of asymptomatic non-fatal PE of about 20%, but the proportion of emboli which are symptomatic is considerably less.

Some patients who have had THR are readmitted after discharge with symptomatic DVT or PE (Bergqvist 1993); this raises the question of prolonged prophylaxis. The only available figure for the proportion readmitted was provided by the Oxford Record Linkage study; 0.73% needed readmission with venous thrombosis or embolism within 28 days of discharge (Seagroatt et al 1991).

We have studied a large cohort of patients who did not have routine chemical prophylaxis to determine the incidence of clinical thromboembolism before and after discharge, and the mortality from PE.

PATIENTS AND METHODS

We reviewed all the records of 1112 patients who had had 1162 primary or revision THR performed in the years 1990 and 1991. The patients were treated at one specialised centre by 12 consultant-led surgical teams, serving a population of about one million. There were 18 bilateral procedures, and 112 revision operations. Fifty patients had two replacements within the two-year period.

The standard practice was to use antiembolism stockings and early mobilisation. The choice of general, epidural or spinal anaesthesia was made by the anaesthetist, and pos-

Table I. Questionnaire sent to all patients

Has the above-named died since leaving hospital? YES/NO
If YES, what was the date, place and cause?
Did you have any problems while in hospital, especially:
thrombosis of the leg requiring a heparin drip or warfarin tablets:
embolism, that is shortness of breath, chest pain, or sudden collapse;
transferral to Bristol Royal Infirmary for a special injection x-ray of your leg or chest?
Did you have any problems in the few months after leaving hospital, such as:
swollen or painful calf;
chest pain;
shortness of breath?
Did you have to go to hospital for a leg-injection x-ray?
Have you been readmitted to hospital for:
swollen, painful leg (e.g. clot or thrombosis);
heart problems (e.g. heart attack);
lung problems (e.g. thrombosis, clot, embolism)?
If so:
which hospital;
which consultant;
what was the treatment?
Have you ever had a heparin drip or warfarin tablets since the hip operation?
If so, approximately how long after the operation were they started?

terior, lateral and anterolateral approaches were used. Anti-coagulant prophylaxis was not used routinely, but was reserved for those considered to be at the greatest risk of thromboembolism.

A questionnaire (Table I) was sent to 1087 patients at least six months after the operation, and followed by a second questionnaire if no response was received within two months (excluding 25 who were known to have died). Failure to respond to the second questionnaire led to a third questionnaire; if this was not returned an alternative address was sought through the general practitioner or Family Health Services Authority. The full hospital records of residual non-responders were then retrieved and studied.

If a patient had died or the questionnaire showed *any* suggestion of a thromboembolic event or the use of oral anticoagulants, the hospital records were retrieved. Death within six months was assumed to be potentially related to the operation and its cause was established by reference to the post-mortem record or death certificate.

To validate the accuracy of the questionnaire a random sample of 109 medical records (10%) of those with questionnaire responses which were negative for thromboembolic events was scrutinised for any evidence of such events.

We have given 95% confidence intervals where they are

appropriate, using the formula for the standard error of a proportion based on the normal approximation of the Poisson distribution.

RESULTS

All 1112 patients were traced.

Validation of questionnaire. No deaths or thromboembolic episodes were identified in the clinical records of the random sample of 109 patients who had returned a negative questionnaire. All of this sample cohort had used anti-embolism stockings. Spinal or epidural anaesthesia had been given to 59.6% and prophylactic anticoagulants to 10.6%.

The positive predictive value (true positive divided by total positive) of the questionnaire for proven thromboembolism was 50.6% (40/79).

There were 40 non-responders (42 THRs) of whom two had died at least one year after surgery and two had been readmitted, one for a venogram which was normal, and one for a V/Q scan which was positive. The total morbidity from thromboembolic complications was 3.4% (95% CI 2.5% to 4.7%).

Deaths (Table II). Seventeen patients (1.46% of procedures) had died within six months of surgery, none of them after bilateral THR. One patient died at seven months; he

Table II. Deaths within six months of total hip replacement

Day of death	Age of patient (yr)	Post-mortem	Death certificate
1	78	Pulmonary embolism	
2	68	Pulmonary embolism	
2 R*	80	Myocardial infarct, congestive cardiac failure	
2	75	Myocardial infarct	
5	73	Pulmonary embolism	
5	80	Myocardial infarct	
15†	87	Myocardial infarct	
20	80	Left ventricular failure	
		Pneumonia	
21	67		Bronchopneumonia
			Septic THR
25 R*	80		Cerebrovascular accident
38	71		Peritonitis
			Perforated duodenal ulcer
40†	70	Pulmonary embolism, DVT	
42†	74	Myocardial infarct	
52†		Haemorrhage from oesophageal ulcer	
60	74		Bronchopneumonia
			Cerebrovascular accident
160†	75		Carcinoma of pancreas
180†		Carcinoma of pancreas	

* R, revision THR

† after leaving hospital

had been readmitted 12 days postoperatively with an isolated proximal thrombosis and was anticoagulated for three months. At six months he was admitted with a myocardial infarct and subsequent PE. He was again anticoagulated and died one month later from the complications of gastrointestinal haemorrhage.

Fatal pulmonary embolism (Table II). Four patients died from pulmonary embolism, three as inpatients and one after discharge. The patient who died after discharge had had DVT after a cholecystectomy 16 years previously, and had been given a six-week course of warfarin started on the second day after THR. The course had been stopped four days before his death. The rate of fatal PE was therefore

4/1162 (0.34%, CI 0.09 to 0.88) and the rate of fatal PE after discharge was 1/1151 (0.087%, CI 0 to 0.48).

Pulmonary embolism (Table III). Nine patients had an inpatient V/Q scan, which was positive for PE in six. Nine patients were readmitted for a V/Q scan, which was positive for PE in eight. The overall incidence of symptomatic, proven PE was 14/1162 (1.20%, CI 0.657 to 2.02), and the readmission rate for proven PE was 8/1151 (0.7%, CI 0.30 to 1.36). The average delay between the onset of symptoms and the V/Q scan was 2.4 days (0 to 9). Two patients were readmitted with painful legs; they had venography with negative results, but further symptoms led to positive V/Q scans for PE on the following day.

Table III. Details of patients having pulmonary embolism

Case	Age (yr)	Day		Discharge	Readmission	Spinal or epidural anaesthetic	Anti-coagulant prophylaxis
		Onset of symptoms	V/Q scan				
1	56	3	7				
2	59	4	5				
3	74	4	7				
4	74	7	8				
5	73	7	8			+	
6	72	9	18	12		+	
7	63	11	11	10	+		
8	76	14	20	14	+		
9	63	17	17	9	+	+	
10	67	17	17	13	+	+	
11	71	17	19	18	+	+	+
12	68	20	20	13	+	+	
13	78	27	33	14	+		
14	57	36	36	7	+	+	

Table IV. Details of patients having deep-vein thrombosis

Case	Age (yr)	Day		Readmission	Type of thrombosis	Spinal or epidural anaesthetic	Anti-coagulant prophylaxis
		Onset of symptoms	Venogram				
1	73	3	5		Calf and isolated femoral	+	
2	76	6	8		Calf		
3	78	7	10		Full leg	+	
4	73	7	12		Calf and isolated femoral		
5	76	7	8		Minor calf		
6	53	9	18	8	Calf and popliteal	+	
7	68	10	10		Calf and popliteal	+	
8	68	10	11		Isolated femoral		
9	66	10	11		Full leg		
10	77	10	14	11	Isolated femoral		
11	74	12	14	10	Isolated femoral		
12	46	14	15	10	Full leg		
13	59	14	19	7	Full leg	+	
14	61	15	15	8	Full leg		
15	65	15	21	13	Calf		
16	81	20	23		Full leg		+
17	75	20	40	11	Full leg		
18	49	28	28	10	Minor calf	+	
19	73	35	50	9	Full leg		
20	71	40	40	11	Full leg		
21	58	140	150	11	Full leg		+
22	73	150	150	13	Full leg	+	+

Deep-vein thrombosis (Table IV). Fourteen patients had inpatient venograms: nine were positive for DVT, at an average delay between the onset of symptoms and the venogram of four days (0 to 20). A total of 23 symptomatic patients were readmitted for venography: 13 were positive and 10 were negative. The overall venographically-proven DVT rate was therefore 22/1162 (1.89%, CI 1.11 to 2.76), and the readmission rate for proven DVT was 13/1151 (1.13%, CI 0.60 to 1.93).

Five patients had anticoagulants prescribed empirically for DVT without venographic proof. One patient who presented with a DVT after 140 days had dislocated her prosthesis at two weeks, had then been placed in a brace for eight weeks and given low-dose heparin for one week. One patient who presented with DVT after 150 days had been taking adjusted-dose warfarin for three months after THR, because of a history of previous DVT.

DISCUSSION

We consider that the comprehensive follow-up, the high post-mortem rate for the early deaths and the high negative predictive value of the questionnaire have confirmed the validity of our results.

Our inpatient, all-cause mortality rate of 0.86% (10/1162) compares with the 0.63% reported by Sheppard et al (1981) and the 90-day mortality rate of 1.3% (15/1162) compares with the 1.1% reported by Seagroatt et al (1991). It is clear from all three studies that the oft-quoted PE mortality figures of 2.3% to 3.4% after THR are misleading. It should be noted that our patients and those reported from Oxford by Seagroatt et al (1991) were not

routinely given chemical antithrombotic prophylaxis. The rate of 0.34% of fatal PE which we found represents 100 deaths for the 30 000 THRs performed annually in England; and the upper confidence limit of 0.88% suggests 265 deaths per annum.

Prophylaxis against thromboembolism remains controversial. Despite considerable pressure from lawyers and from other branches of the medical profession (Parker-Williams and Vickers 1991; Campling et al 1993), many orthopaedic surgeons are reluctant to use chemical prophylaxis because of doubts about efficacy and possible haemorrhagic complications (Owen and Coorsh 1992). Charnley abandoned the use of adjusted-dose phenindione because the benefit from reduction of PE mortality was matched by an increased mortality from gastrointestinal haemorrhage (Crawford, Hillman and Charnley 1968). Coventry et al (1973) recommended delay in warfarin anticoagulation to the fifth postoperative day but this would have failed to cover three of the four fatal PE which we report. Meta-analysis shows that both low-dose, unfractionated heparin and low-molecular-weight heparin substantially reduce the incidence of venographic DVT after THR from about 45% to about 23% (Collins et al 1988) and about 19% (Jørgenson, Wille-Jørgenson and Hauch 1993), although with some haemorrhagic side-effects. This reduction in DVT has been extrapolated to imply a reduction in incidence of fatal PE, but no study has been powerful enough to demonstrate directly such a reduction after THR. It would require a randomised study of 28 000 patients to show halving of the fatal PE rate from 0.34% to 0.17% at the 95% significance level with 80% power.

Seagroatt et al (1991) report a readmission rate for

symptomatic thromboembolic complications of 0.73% within 28 days of discharge after THR; our rate for the same period was 1.39% (CI 0.65 to 1.95, 16/1151 surviving patients). It is uncertain whether the thrombi leading to readmission were present but symptomless at the time of discharge or whether they developed later. There is no evidence to suggest that prolonged prophylaxis may influence such late complications, and no cost-benefit or risk-benefit studies have been published to support such a policy.

Various factors complicate the design of any study which aims to assess the efficacy of thromboprophylaxis after hospital discharge. It is known that venous thrombosis can occur despite normal venography on discharge if anticoagulation is stopped on leaving hospital (Matzsch et al 1990; Tremaine, Choroszy and Menking 1991), and the possibility of rebound thrombosis after stopping prophylaxis has been identified by sequential ^{131}I studies (Sikorski, Hampson and Staddon 1981). There are no data on which to base rational timing for repeated screening for asymptomatic thromboembolism after discharge, and patients may not comply with a protocol requiring repeated injections of anticoagulant once inpatient supervision has ended.

The problem of postoperative leg swelling and its relationship to DVT after THR has not been studied.

Conclusions. The fatal PE rate after THR with selective chemical prophylaxis was low but nevertheless represented from 100 up to 265 deaths in England each year. A very large randomised clinical trial would be required to demonstrate directly whether any prophylactic measure could reduce this rate further; reliance on the indirect marker of DVT is therefore more feasible. There was a discrepancy between the high DVT rate shown by universal screening venography and the clinical DVT rate demonstrated in this study. The total early morbidity from thromboembolic disease was considerable (3.4%); prophylaxis to reduce this would be justifiable if the complications of such prophylaxis did not produce an alternative morbidity. There is insufficient evidence to recommend thromboprophylaxis after discharge from hospital.

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