

THROMBOPROPHYLAXIS AND DEATH AFTER TOTAL HIP REPLACEMENT

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The recommendation that patients having a total hip replacement should receive pharmacological thromboprophylaxis is based on the belief that fatal pulmonary embolism is common, and that prophylaxis will decrease the death rate. To investigate these assumptions we performed a meta-analysis of all studies on hip replacement which included information about death or fatal pulmonary embolism. A total of 130 000 patients was included. The studies were so varied in content and quality that the results of our analysis must be interpreted with some caution.

The fatal pulmonary embolism rate was 0.1% to 0.2% even in patients who received no prophylaxis. This is an order of magnitude lower than that which is generally quoted, and therefore the potential benefit of prophylaxis is small and may not justify the risks. To balance the risks and benefits we must consider the overall death rate. This was 0.3% to 0.4%, and neither heparin nor any other prophylactic agent caused a significant decrease.

Our study demonstrates that there is not enough evidence in the literature to conclude that any form of pharmacological thromboprophylaxis decreases the death rate after total hip replacement. For this reason guidelines which recommend their routine use to prevent death after hip replacement are not justified.

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Despite strong pressure from both scientific and pharmaceutical sources, orthopaedic surgeons have been very slow to adopt the recommendation that all patients undergoing total hip replacement (THR) should be given some form of thromboprophylaxis (Brenkel and Clancy 1989; Laverick, Croal and Mollan 1991; Campling et al 1993; Unwin, Harries and Jones 1995).

The National Institutes of Health (NIHCC 1986), the Thromboembolic Risk Factors (Lowe et al 1992) and the European Consensus conferences (ECC 1992) all classified THR as a high-risk procedure, which implies a fatal pulmonary embolism (PE) rate of 1% to 10%. On this basis they recommend that some form of heparin should be used as prophylaxis. The risk factors for hip replacement, however, differ from those for other types of surgery (Salzman and Harris 1976; Murray, Carr and Bulstrode 1995), and it is necessary, before guidelines are agreed, that the risks and benefits of any prophylactic regime are weighed up in terms of mortality and morbidity after THR. No previous studies of mortality after THR have been large enough to compare the risks and benefits of various prophylactic regimes. The available data on the effect of prophylaxis on morbidity from thromboembolism after THR are sparse and conflicting: it is not even clear whether postphlebotic limb and leg ulcers are a genuine problem (Moore and Freeman 1993; McNally et al 1994; Warwick et al 1996), and there are no trials which have assessed the effect of prophylaxis on these outcomes. There is also a risk that prophylactic anticoagulation may increase the rate of deep infection (Kong 1995).

Many randomised controlled trials have demonstrated a significant reduction in the incidence of *venographic* deep-vein thrombosis (DVT) after THR when various prophylactic agents are used (Imperiale and Speroff 1994). These trials are relatively easy to perform: they require only small numbers of patients because of the high incidence of asymptomatic DVT of 40% to 80%, so that the effect observed is large. It has been assumed that this reduction in DVT rate will lead to a similar fall in the overall death rate. This may be a false assumption if fatal pulmonary embolism is not very common and does not account for most deaths, if a fall in the DVT rate is not associated with a similar fall in the fatal PE rate, or if prophylaxis increases the risk of other causes of death.

We aimed to use meta-analysis to determine as accurately as possible the actual mortality after THR and to

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Table I. The fatal PE and death rates with confidence limits (CL) in trials starting in different decades, with the death rate in 1991-2 in the UK calculated from the number of deaths identified by the National Confidential Enquiry into Perioperative Deaths (NCEPOD) (Campling et al 1993) and the number of THRs implanted during that period (Williams et al 1994)

Start of trial	Fatal PE	Patients	Rate (%)	95% Confidence limits	Deaths	Patients	Rate (%)	95% Confidence limits
1960s	129	20 190	0.64	0.53 to 0.75	237	21 501	1.10	0.96 to 1.24
1970s	143	40 207	0.36	0.30 to 0.41	434	39 199	1.11	1.00 to 1.21
1980s and 90s	27	23 511	0.11	0.07 to 0.16	69	18 204	0.38	0.29 to 0.47
NCEPOD					134	38 000	0.35	0.29 to 0.41

Table II. The fatal PE (FPE) rate for different types of prophylaxis in studies starting in the 1970s, 80s and 90s. Differences between groups do not quite reach statistical significance ($p = 0.051$)

Prophylaxis	FPE	Patients	Rate (%)	95% Confidence limits
None	4	3432	0.12	0.03 to 0.30
Heparin	8	10 356	0.08	0.03 to 0.15
Warfarin	2	5162	0.04	0.00 to 0.14
Aspirin	3	2700	0.11	0.02 to 0.32
Dextran	7	2730	0.26	0.10 to 0.53

attempt to weigh up the risks and benefits of various types of thromboprophylaxis in terms of total mortality.

MATERIALS AND METHODS

We performed a meta-analysis of all available studies of THR in which information about overall death rate or fatal PE had been included. We searched for all papers on the outcome of THR in which the number of patients being studied and the total number of deaths or of fatal cases of PE had been reported. The Medline bibliographic database was reviewed from 1966 to 1995 to identify all the relevant English language literature. References mentioned in consensus documents, previous meta-analyses or other papers were also traced. No attempt was made to restrict the search to controlled trials or even to prospective trials. The data were used only once when the outcome of the same group of patients had been reported in more than one paper.

We recorded the year in which the trial was started, the number of patients involved, the number of cases of fatal PE and the number of deaths occurring within three months after the operation, since it is known that after THR the death rate is elevated for no more than three months (Seagroatt et al 1991). We subdivided the type of prophylaxis into six categories: none, heparin, warfarin, aspirin, dextran and others. The 'none' group included those given no prophylaxis, placebo, and antiembolism stockings. The 'heparin' group included those given any form of heparin, heparinoid or low-molecular-weight heparin prophylaxis, with or without stockings. The 'warfarin', 'aspirin' and 'dextran' groups were also with or without stockings. The other group included all trials in which a mixture or combination of these prophylactic regimes had been used,

trials with other prophylactic agents, and trials in which the prophylactic regime was unclear. This group included patients treated by mechanical pumps as the number in this subgroup (745) was too small for a separate analysis.

We have quoted 95% confidence limits (CL); in subgroups in which the number of deaths occurring was small the confidence limits were determined using the Poisson distribution (Pearson and Hartley 1966). The significance of differences between subgroups was determined using the chi-squared test.

RESULTS

We identified 181 papers containing usable information about 93 000 patients (see reference list). The reports show a progressive decrease in both fatal PE and death rates over the last three decades (Table I). During the last 15 years the overall death rate has been 0.38% (CL 0.29% to 0.47%) and the fatal PE rate has been 0.11% (CL 0.07% to 0.16%) (Table I).

Additional information about the current death rate in the UK can be obtained by dividing the number of deaths (134) identified by the National Confidential Enquiry into Perioperative deaths 1991-2 (NCEPOD) (Campling et al 1993) by the number of THRs implanted during that period (38 000) (Williams et al 1994) (Table I).

The fatal PE rate, the overall death rate and the non-PE death rate for the different types of prophylaxis in studies starting in the 1970s, 80s and 90s are shown in Tables II, III and IV, respectively. Information from only 22 000 patients was suitable for inclusion in these analyses. The number of fatal PE in each subgroup is small and there is no statistically significant difference between the groups. Neither heparin nor any other prophylactic agent caused a sig-

Table III. The death rate for different types of prophylaxis in studies starting in the 1970s, 80s and 90s. Differences between groups are not statistically significant ($p = 0.2$)

Prophylaxis	Deaths	Patients	Rate (%)	95% Confidence limits
None	10	3355	0.30	0.14 to 0.55
Heparin	40	10 105	0.40	0.28 to 0.54
Warfarin	11	3763	0.29	0.15 to 0.52
Aspirin	4	2649	0.15	0.04 to 0.39
Dextran	13	2618	0.50	0.26 to 0.85

Table IV. The non-pulmonary embolus death (NPED) rate for different types of prophylaxis in studies starting in the 1970s, 80s and 90s. Differences between groups are not significant ($p = 0.14$). The only papers that could be used to determine the non-pulmonary embolus death rate were those which included information about total deaths and fatal PE. This explains why the data in Tables II, III and IV appear to be inconsistent

Prophylaxis	NPED	Patients	Rate (%)	95% Confidence limits
None	7	3355	0.21	0.08 to 0.43
Heparin	32	10 105	0.32	0.22 to 0.44
Warfarin	9	3763	0.24	0.11 to 0.45
Aspirin	1	2649	0.04	0.00 to 0.21
Dextran	6	2618	0.23	0.08 to 0.50

nificant decrease in the overall death rate compared with no prophylaxis. Compared with heparin the use of aspirin caused a significant decrease in non-PE deaths ($p = 0.01$). As a result its use tended to decrease the overall death rate, although this did not quite reach statistical significance ($p = 0.052$).

DISCUSSION

In the introduction to many of the papers which we reviewed, the importance of the subject was emphasised by stating that the fatal PE rate after THR is above 1%. This accepted wisdom, which is supported by the three consensus documents (NIHCC 1986; ECC 1992; Lowe et al 1992), is based on a few studies conducted mainly in the 1960s (Coventry et al 1973; Johnson, Green and Charnley 1977). Our review of a large proportion of the published data demonstrates that even in the 1960s the fatal PE rate was less than 1%. Since then it has progressively decreased and during the last 15 years has been reported to be between 0.07% and 0.16% which is an order of magnitude lower than generally perceived. Even in the subgroup of papers reporting results with no pharmacological thromboprophylaxis the rate for fatal PE is still only one or two per thousand (0.12%, CL 0.03% to 0.3%). It therefore seems likely that the progressive fall in the fatal PE rate is predominantly the result of improved surgical, anaesthetic and rehabilitation techniques rather than the increased use of thromboprophylaxis. The current fatal PE rate and there-

fore the potential benefit of thromboprophylaxis appear to have been grossly overestimated. The benefit may be so low that it is similar to the risks of the therapy.

It is not always possible to determine if a death is caused by pulmonary embolus and as a result the rate for fatal PE may be inaccurate (Fitts et al 1964). It is therefore important to determine the overall death rate. This sets an upper limit to the fatal PE rate, and is also essential to balance the risks and benefits (Warwick and Freeman 1995).

Our meta-analysis suggests that the overall death rate is 0.38% (CL 0.29% to 0.47%). In the papers which we reviewed the deaths were assessed for different periods after the THR, high-risk patients were often excluded, and many of the studies came from centres of excellence. It could therefore be argued that the meta-analysis gives a false impression of the overall death rate after THR. A further potential bias is that in many of the trials the patients were screened by venography. A positive result may have resulted in the patient being formally anticoagulated which may have influenced the mortality. The death rate calculated from NCEPOD data and national statistics (0.35%, CL 0.29% to 0.41%, Table I), however, is similar to that found in our meta-analysis (0.38%, CL 0.29% to 0.47%). This suggests that the potential biases in the meta-analysis are not important and that a combination of both sets of data may give a better estimate of the current overall death rate after THR: this estimate is 0.36% (CL 0.31% to 0.41%).

To extract as much data from the literature as possible we undertook an opportunist meta-analysis (Rosendaal 1994) which was not restricted to randomised controlled trials. An opportunist meta-analysis includes data from studies in which the primary aim is different from the aim of the meta-analysis: we investigated death rates although many of the papers were studies of rates of DVT. Such an opportunist meta-analysis minimises some of the potential weaknesses of formal meta-analysis, such as publication bias against negative results or commercial bias against unfavourable results. Classical meta-analysis combines data from randomised controlled trials which compare the same pair of treatments. In our meta-analysis data were pooled from trials involving many different comparisons. This type of meta-analysis has previously been used to study thromboprophylaxis after THR (Imperiale and Speroff 1994) and the results must be interpreted with considerable caution, since pooling is based on the assumption that patients and their management are similar in different studies. For example, if the type of prophylaxis changed with time then an observed difference between prophylactic regimes may be explained by a progressive decrease in mortality rather than a real difference between the regimes.

Despite using all the relevant data from a large number of papers, we have been unable to draw any firm statistical conclusions about the type of thromboprophylaxis which should be used, and even whether it should be used at all. To demonstrate a significant reduction in the incidence of

fatal PE would require about 30 000 patients in each arm of a trial (Murray et al 1995; Warwick, Williams and Bannister 1995), which is substantially more than the number of patients in each of our meta-analyses.

If no pharmacological thromboprophylaxis is used the fatal PE rate after THR appears to be about 0.12%. Previous meta-analyses from all fields of medicine and surgery have suggested that both heparin and aspirin cause a substantial decrease in this rate (Collins et al 1988; APT 1994b). If we assume that prophylaxis is effective at preventing fatal PE after THR then our data would suggest that such prophylaxis would not decrease the fatal PE rate after THR by more than 0.05%. Anticoagulants do have a complication rate although the death rate from these complications is not known (Kong 1995; Warwick and Freeman 1995). If the death rate due to anticoagulant complications is 0.05% or more then the use of these agents will actually cause harm. The best method to assess whether a prophylactic agent is useful is to consider the overall death rate: this takes into account both risks and complications (Warwick and Freeman 1995). In our meta-analysis neither heparin nor any other prophylactic agent caused a significant decrease in overall death rate compared with no prophylaxis. There is therefore as yet no good evidence that any pharmacological agent does more good than harm after a routine THR. It is likely, however, that there is a subgroup of patients, as yet poorly defined, which would benefit from aggressive thromboprophylaxis.

If, despite the finding that no agent significantly decreases the overall death rate, orthopaedic surgeons feel that they should use some form of pharmacological prophylaxis then it would seem appropriate to compare different agents. Heparin has the most evidence suggesting that it should decrease the fatal PE rate (NIHCC 1986; ECC 1992; Lowe et al 1992). Aspirin may be a better option, however, as this meta-analysis suggests that, compared with heparin, aspirin causes a decrease in non-PE deaths, and as a result shows a tendency to decrease the overall death rate. There is also evidence from large trials unrelated to hip replacement that aspirin prevents non-PE deaths (APT 1994a).

We believe that in future pharmaceutical companies and others concerned with the study of thromboembolism should put the subject into perspective by using up-to-date, reliable data based on large numbers of patients. Every effort should be made to avoid the assumption, until clear evidence is available to the contrary, that a reduction in DVT rate will automatically reduce the overall death rate. Even for elective total hip replacement, for which there are large numbers of outcome studies of a common and reasonably standard procedure, there is still not enough information on which to draw up guidelines on thromboprophylaxis. Until a randomised controlled trial of adequate size can be performed, using morbidity and mortality as the main outcome measures, the problem is likely to remain unresolved.

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REFERENCES * references not used in the meta-analysis

- Alfaro MJ, Paramo JA, Rocha E.** Prophylaxis of thromboembolic disease and platelet-related changes following total hip replacement: a comparative study of aspirin and heparin-dihydroergotamine. *Thromb Haemost* 1986;56:53-6.
- Alexander JP, Barron DW.** Clinical considerations in anaesthesia for hip arthroplasty. *Anaesthesia* 1978;33:748-51.
- Alexander JP, Barron DW.** The effect of alcohol on the pulmonary embolic syndrome. *Anaesthesia* 1980;35:506-8.
- Amstutz HC, Friscia DA, Dorey F, Carney BT.** Warfarin prophylaxis to prevent mortality from pulmonary embolism after total hip replacement. *J Bone Joint Surg [Am]* 1989;71-A:321-6.
- ***APT.** Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy-i: prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *Br Med J* 1994a;308:81-106.
- ***APT.** Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy-iii: reduction in venous thrombosis and pulmonary embolism by antiplatelet prophylaxis among surgical and medical patients. *Br Med J* 1994b;308:235-46.
- Arborelius M, Fredin H, Nyman U, Hellekant C.** Angiographic evaluation of scintigraphic abnormalities in screening for pulmonary embolism after total hip replacement. *Acta Radiol Diagn Stockh* 1985;26:511-8.
- Atichartakarn V, Pathepochiwong K, Keorochana S, Eurvilaichit C.** Deep vein thrombosis after hip surgery among Thai. *Arch Intern Med* 1988;148:1349-53.
- Bailey JP, Kruger MP, Solano FX, Zajko AB, Rubash HE.** Prospective randomized trial of sequential compression devices vs low-dose warfarin for deep venous thrombosis prophylaxis in total hip arthroplasty. *J Arthroplasty* 1991;6Suppl:S29-35.
- Barber HM, Feil EJ, Galasko CSB, et al.** A comparative study of dextran-70, warfarin and low-dose heparin for the prophylaxis of thrombo-embolism following total hip replacement. *Postgrad Med J* 1977;53:130-3.
- Barnes RW, Brand RA, Clarke W, Hartley N, Hoak JC.** Efficacy of graded-compression antiembolism stockings in patients undergoing total hip arthroplasty. *Clin Orthop* 1978;132:61-7.
- Beisaw NE, Comerota AJ, Groth HE, et al.** Dihydroergotamine/heparin in the prevention of deep-vein thrombosis after total hip replacement: a controlled, prospective, randomized multicenter trial. *J Bone Joint Surg [Am]* 1988;70-A:2-10.
- Belch JJ, Meek DR, Lowe GD, et al.** Subcutaneous anecrod in prevention of deep vein thrombosis after hip replacement surgery. *Thromb Res* 1982;25:23-31.
- ***Brenkel IJ, Clancy MJ.** Total hip replacement and anti thrombotic prophylaxis. *Br J Hosp Med* 1989;42:282-4.
- Brown JG, Ward PE, Wilkinson AJ, Mollan RAB.** Impedance plethysmography: a screening procedure to detect deep vein thrombosis. *J Bone Joint Surg [Br]* 1987;69-B:264-7.
- ***Campling EA, Devlin HB, Hoile RW, Lunn JN.** *The Report of the National Confidential Enquiry into Perioperative Deaths 1991/1992.* NCEPOD, London.
- Charnley J.** The long-term results of low-friction arthroplasty of the hip performed as a primary intervention. *J Bone Joint Surg [Br]* 1972;54-B:61-76.
- Chiapuzzo E, Orenco GB, Ottria G, et al.** The use of low molecular weight heparins for post-surgical prevention in orthopaedic patients. *J Int Med Res* 1988;16:359-66.
- Christensen SW, Wille-Jorgensen P, Bjerg-Nielsen A, Kjaer L.** Prevention of deep venous thrombosis following total hip replacement, using epidural analgesia. *Acta Orthop Belg* 1989;55:58-61.
- ***Collins R, Scrimgeour A, Yusuf S, Peto R.** Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin: an overview of results of randomized trials in general, orthopaedic and urological surgery. *N Engl J Med* 1988;18:1162-73.

- Colville J, Raunio P.** Charnley low-friction arthroplasties of the hip in rheumatoid arthritis: a study of the complications and results of 378 arthroplasties. *J Bone Joint Surg [Br]* 1978;60-B:498-503.
- Colwell CW, Spiro TE, Trowbridge AA, et al.** Use of Enoxaparin, a low-molecular-weight heparin, and unfractionated heparin for the prevention of deep venous thrombosis after elective hip replacement. *J Bone Joint Surg [Am]* 1994;76-A:3-14.
- Cooke ED, Bowcock SA, Pilcher MF, et al.** Serum fibrin(ogen) degradation products in diagnosis of deep-vein thrombosis and pulmonary embolism after hip surgery. *Lancet* 1975;2:51-4.
- Cooke ED, Dawson MHO, Ibbotson RM, et al.** Failure of orally administered hydroxychloroquine sulphate to prevent venous thromboembolism following elective hip operations. *J Bone Joint Surg [Am]* 1977;59-A:496-500.
- Coventry MB, Nolan DR, Beckenbaugh RD.** 'Delayed' prophylactic anticoagulation: a study of results and complications in 2012 total hip arthroplasties. *J Bone Joint Surg [Am]* 1973;55-A:1487-92.
- D'Ambrosia RD, Lipscomb PR, McClain EJ, Wissinger HA, McDowell JH.** Prophylactic anticoagulation in total hip replacement. *Surg Gynecol Obstet* 1975;140:523-7.
- Dall D.** Early results of total hip joint replacement. *S Afr Med J* 1974;48:1979-84.
- Davis FM, Laurenson VG, Gillespie WJ, Wells JE, Foate J, Newman E.** Deep vein thrombosis after total hip replacement: a comparison between spinal and general anaesthesia. *J Bone Joint Surg [Br]* 1989;71-B:181-5.
- Dechavanne M, Ville D, Berruyer M, et al.** Randomised trial of a low-molecular-weight heparin (Kabi 2165) versus adjusted-dose subcutaneous standard heparin in the prophylaxis of deep venous thrombosis after elective hip surgery. *Haemostasis* 1989;19:5-12.
- DESG.** Danish Enoxaparin Study Group: low-molecular-weight heparin (Enoxaparin) vs dextran 70. *Arch Intern Med* 1991;151:1621-4.
- DiSerio FJ, Parno J, Singer JM.** Limitation of impedance plethysmography in assessing efficacy of dihydroergotamine-heparin prophylaxis of deep vein thrombosis. *Thromb Res* 1985;37:449-58.
- ***ECC.** *European consensus statement on the prevention of venous thromboembolism.* London: Med-Orion, 1992.
- Eriksson BI, Eriksson E, Risberg B.** Impaired fibrinolysis and post-operative thromboembolism in orthopaedic patients. *Thromb Res* 1991;62:55-64.
- Eriksson BI, Kälébo P, Anthmyr BA, et al.** Prevention of deep vein thrombosis and pulmonary embolism after total hip replacement. *J Bone Joint Surg [Am]* 1991;73-A:484-93.
- Eriksson BI, Kälébo P, Risberg B.** Clinical experience of a low molecular weight heparin (Fragmin) in the prevention of thromboembolism after total hip replacement. *Semin Thromb Haemost* 1993;19:Suppl 1:122-7.
- Eriksson BI, Zachrisson BE, Teger-Nilsson A-C, Risberg B.** Thrombosis prophylaxis with low molecular weight heparin in total hip replacement. *Br J Surg* 1988;75:1053-7.
- Estoppey D, Hochreiter J, Breyer HG, et al.** Org 10172 (Lomoparan) vs heparin-dhe in prevention of thromboembolism in total hip replacement: a multicentre trial. *Thromb Haemost* 1989;62:356.
- Evarts ME, Feil EJ.** Prevention of thromboembolic disease after elective surgery of the hip. *J Bone Joint Surg [Am]* 1971;53-A:1271-80.
- ***Fitts WT, Lehr HB, Bitner RL, Spelman JW.** An analysis of 950 fatal injuries. *Surgery* 1964;56:663-8.
- Flicotaux H, Kher A, Jean N, et al.** Comparison of low dose heparin and low dose heparin combined with aspirin in prevention of deep vein thrombosis after total hip replacement. *Pathol Biol Paris* 1977;25:Suppl 55-8.
- Flordal PA, Ljungstrom K-G, Svensson J, Ellman B, Neander G.** Effects on coagulation and fibrinolysis of desmopressin in patients undergoing total hip replacement. *Thromb Haemost* 1991;66:652-6.
- Fordey MJ, Baker AS, Staddon GE.** Efficacy of fixed minidose warfarin prophylaxis in total hip replacement. *BMJ* 1991;303:219-20.
- Fordey MJ, Ling RSM.** A venous foot pump reduces thrombosis after total hip replacement. *J Bone Joint Surg [Br]* 1992;74-B:45-9.
- Francis CW, Marder VJ, Evarts CM.** Lower risk of thromboembolic disease after total hip replacement with non-cemented than with cemented prostheses. *Lancet* 1986;1:769-71.
- Francis CW, Marder VJ, Evarts CM, Yaoukoolbodi S.** Two-step warfarin therapy: prevention of postoperative venous thrombosis without excessive bleeding. *JAMA* 1983;249:374-8, 2021 (correction).
- Francis CW, Pellegrini VD, Marder VJ, et al.** Prevention of venous thrombosis after total hip arthroplasty. *J Bone Joint Surg [Am]* 1989;71-A:327-35.
- Francis CW, Pellegrini VD, Marder VJ, et al.** Comparison of warfarin and external pneumatic compression in prevention of venous thrombosis after total hip replacement. *JAMA* 1992;267:2911-5.
- Fredin H, Bergqvist D, Cederholm C, Lindblad B, Nyman U.** Thromboprophylaxis in hip arthroplasty: dextran with graded compression or preoperative dextran compared in 150 patients. *Acta Orthop Scand* 1989;60:678-81.
- Fredin H, Nilsson B, Rosberg B, Tengborn L.** Pre- and postoperative levels of antithrombin III with special reference to thromboembolism after total hip replacement. *Thromb Haemost* 1983;49:158-61.
- Fredin H, Rosberg B.** Anaesthetic techniques and thromboembolism in total hip arthroplasty. *Eur J Anaesthesiol* 1986;3:273-81.
- Fredin HO.** Screening and treatment of pulmonary embolism after total hip replacement. *Acta Orthop Scand* 1983;54:164-7.
- Fredin HO, Nillius AS.** Fatal pulmonary embolism after total hip replacement. *Acta Orthop Scand* 1982;53:407-11.
- Fredin HO, Rosberg B, Arborelius M, Nylander G.** On thromboembolism after total hip replacement in epidural analgesia: a controlled study of dextran 70 and low-dose heparin combined with dihydroergotamine. *Br J Surg* 1984;71:58-60.
- Freeman PA, Lee P, Bryson TW.** Total hip joint replacement in osteoarthritis and polyarthritis. *Clin Orthop* 1973;95:224-30.
- Frick H, Haas S.** Prevention of deep vein thrombosis by low-molecular-weight heparin and dihydroergotamine in patients undergoing total hip replacement. *Thromb Res* 1991;63:133-43.
- Gallus A, Raman K, Darby T.** Venous thrombosis after elective hip replacement: the influence of preventive intermittent calf compression and of surgical techniques. *Br J Surg* 1983;70:17-9.
- Gershuni DH, Axer A, Segal D, Halperin N.** Total hip replacement arthroplasty. *Arch Orthop Unfallchir* 1979;79:217-27.
- Gitel SN, Salvati EA, Wessler S, et al.** The effect of total hip replacement and general surgery on antithrombin III in relation to venous thrombosis. *J Bone Joint Surg [Am]* 1979;61-A:653-6.
- Goss TP, Stinchfield FE, Cosgriff SW.** The efficacy of low-dose heparin-warfarin anticoagulation prophylaxis after total hip replacement arthroplasty. *Clin Orthop* 1979;141:134-7.
- Gray DH, Mackie CE.** The effect of blood transfusion on the incidence of deep vein thrombosis. *Aust NZ J Surg* 1983;53:439-43.
- Guyer RD, Booth RE Jr, Rothman RH.** The detection and prevention of pulmonary embolism in total hip replacement: a study comparing aspirin and low-dose warfarin. *J Bone Joint Surg [Am]* 1982;64-A:1040-3.
- Haas S, Stemberger A, Fritsche HM, et al.** Prophylaxis of deep vein thrombosis in high risk patients undergoing total hip replacement with low molecular weight heparin plus dihydroergotamine. *Arzneimittelforschung* 1987;37:839-43.
- Hamilton LR, Dunn AW, Davis GL.** Experience with total hip replacement at Oschner Clinic. *South Med J* 1975;68:575-9.
- Hampson WGJ, Harris FC, Lucas HK, et al.** Failure of low-dose heparin to prevent deep-vein thrombosis after hip-replacement arthroplasty. *Lancet* 1974;795-7.
- Harris WH.** Preliminary report of results of Harris total hip replacement. *Clin Orthop* 1973;95:168-73.
- Harris WH, Athanasoulis CA, Waltman AC, Salzman EW.** High and low-dose aspirin prophylaxis against venous thromboembolic disease in total hip replacement. *J Bone Joint Surg [Am]* 1982;64-A:63-6.
- Harris WH, Athanasoulis CA, Waltman AC, Salzman EW.** Prophylaxis of deep-vein thrombosis after total hip replacement: Dextran and external pneumatic compression compared with 1.2 or 0.3 gram of aspirin daily. *J Bone Joint Surg [Am]* 1985;67-A:57-62.
- Harris WH, McKusik K, Athanasoulis CA, Waltman AC, Strauss HW.** Detection of pulmonary emboli after total hip replacement using serial C15 O2 pulmonary scans. *J Bone Joint Surg [Am]* 1984;66-A:1388-93.
- Harris WH, Salzman EW, Athanasoulis CA, et al.** Comparison of warfarin, low-molecular-weight dextran, aspirin, and sub-cutaneous heparin in prevention of venous thromboembolism following total hip replacement. *J Bone Joint Surg [Am]* 1974;56:1552-62.
- Harris WH, Salzman EW, Athanasoulis CA, Waltman AC, Desanctis RW.** Aspirin prophylaxis of venous thromboembolism after total hip replacement. *N Engl J Med* 1977;297:1246-9.

- Harris WH, Salzman EW, DeSanctis RW.** The prevention of thromboembolic disease by prophylactic anticoagulation: a controlled study in elective hip surgery. *J Bone Joint Surg [Am]* 1967;49-A:81-9.
- Harris WH, Salzman EW, DeSanctis RW, Coutts RD.** Prevention of venous thromboembolism following total hip replacement: warfarin vs dextran 40. *J Am Med Assoc* 1972;220:1319-22.
- Hartman JT, Pugh JL, Smith RD, et al.** Cyclic sequential compression of the lower limb in prevention of deep venous thrombosis. *J Bone Joint Surg [Am]* 1982;64-A:1059-62.
- Hoek JA, Nurmohamed MT, Hamelynck KJ, et al.** Prevention of deep vein thrombosis following total hip replacement by low molecular weight heparinoid. *Thromb Haemost* 1992;67:28-32.
- Hogevold HE, Hoiseth A, Reikeras O.** Deep vein thrombosis after total hip replacement. *Acta Radiol* 1990;31:571-3.
- Hogevold HE, Hoiseth A, Reikeras O.** Effect of high-dose corticosteroids on the incidence of deep vein thrombosis after total hip replacement. *Arch Orthop Trauma Surg* 1991;111:29-31.
- Hole A, Terjesen T, Breivik H.** Epidural versus general anaesthesia for total hip arthroplasty in elderly patients. *Acta Anaesthesiol Scand* 1980;24:279-87.
- Hu R.** Prophylaxis of deep-vein thrombosis in total hip surgery. *Can J Surg* 1989;32:207-9.
- Hull R, Raskob G, Pineo G, et al.** A comparison of subcutaneous low-molecular weight heparin with warfarin sodium for prophylaxis against deep-vein thrombosis after hip or knee implantation. *N Engl J Med* 1993;329:1370-6.
- Hull RD, Raskob GE, Gent M, et al.** Effectiveness of intermittent pneumatic leg compression for preventing deep vein thrombosis after total hip replacement. *JAMA* 1990;263:2313-7.
- Hume M, Bierbaum B, Kuriakose TX, Suprenant J.** Prevention of postoperative thrombosis by aspirin. *Am J Surg* 1977;133:420-2.
- Hume M, Donaldson WR, Surprenant J.** Sex, aspirin and venous thrombosis. *Orthop Clin North Am* 1978;9:761-7.
- Huo MH, Salvati EA, Sharrock NE, et al.** Intraoperative adjusted-dose heparin thromboembolic prophylaxis in primary total hip arthroplasty. *Clin Orthop* 1992;277:188-96.
- Hurson B, Ennis JT, Corrigan TP, MacAuley P.** Dextran prophylaxis in total hip replacement: a scintigraphic evaluation of the incidence of deep vein thrombosis and pulmonary embolus. *Ir J Med Sci* 1979;148:140-4.
- *Imperiale TF, Speroff T.** A meta-analysis of methods to prevent venous thromboembolism following total hip replacement. *JAMA* 1994;271:1780-5.
- Ishak MA, Morley KD.** Deep venous thrombosis after total hip arthroplasty: a prospective controlled study to determine the prophylactic effect of graded pressure stockings. *Br J Surg* 1981;68:429-32.
- Jennings JJ, Harris WH, Sarmiento A.** A clinical evaluation of aspirin prophylaxis of thromboembolic disease after total hip arthroplasty. *J Bone Joint Surg [Am]* 1976;58-A:926-8.
- Johansson E, Forsberg K, Johnsson H.** Clinical and experimental evaluation of the thromboprophylactic effect of hydroxychloroquine sulfate after total hip replacement. *Haemostas* 1981;10:89-96.
- Johnson R, Carmichael JHE, Almond HGA, Loynes RP.** Deep venous thrombosis following Charnley arthroplasty. *Clin Orthop* 1978;132:24-30.
- Johnson R, Charnley J.** Hydroxychloroquine in prophylaxis of pulmonary embolism following hip arthroplasty. *Clin Orthop* 1979;144:174-7.
- Johnson R, Green JR, Charnley J.** Pulmonary embolism and its prophylaxis following the Charnley total hip replacement. *Clin Orthop* 1977;127:123-32.
- Johnston RC.** Clinical follow-up of total hip replacement. *Clin Orthop* 1973;95:118-26.
- Josefsson G, Dahlqvist A, Bodfors B.** Prevention of thromboembolism in total hip replacement: aspirin versus dihydroergotamine-heparin. *Acta Orthop Scand* 1987;58:626-9.
- Kakkar VV, Corrigan TP, Fossard DP, et al.** Prevention of fatal postoperative pulmonary embolism by low doses of heparin. International multicentre trial. *Lancet* 1975;ii:45-51.
- Kakkar VV, Fok PJ, Murray WJG, et al.** Heparin and dihydroergotamine prophylaxis against thrombo-embolism after hip arthroplasty. *J Bone Joint Surg [Br]* 1985;67-B:538-42.
- Kakkar VV, Stamatakis JD, Bentley PG, Lawrence D, de Haas HA, Ward VP.** Prophylaxis for postoperative deep vein thrombosis: synergistic effect of heparin and dihydroergotamine. *JAMA* 1979;241:39-42.
- Keggi KJ, Huo MH, Zatorski RN.** Anterior approach to total hip replacement: surgical technique and clinical results of our first one thousand cases using non-cemented prosthesis. *Yale J Biol Med* 1993;66:243-56.
- Kim Y-H, Suh J-S.** Low incidence of deep vein thrombosis after cementless total hip replacement. *J Bone Joint Surg [Am]* 1988;70-A:878-82.
- Kim Y-H, Suh J-S, Kim J-Y.** Incidence and clinical significance of deep vein thrombosis after cementless total hip replacement in Korean patient population. *Yonsei Med J* 1987;28:119-25.
- *Kong KC.** Antithrombotic prophylaxis had little effect on overall mortality. *BMJ* 1995;311:572.
- Kristensen SS, Pedersen P, Pedersen NW, Schmidt SA, Kjaersgaard-Andersen P.** Combined treatment with indomethacin and low-dose heparin after total hip replacement: a double-blind placebo-controlled study. *J Bone Joint Surg [Br]* 1990;72-B:447-9.
- Kundel K, Braun W, Scherer A.** Late results of central talus injuries. *Unfallchirurg* 1995;98:124-9.
- Laguardia AM, Caroli GC.** Prevention of deep vein thrombosis in orthopaedic surgery: comparison of two different treatment protocols with low molecular weight heparin ('Fluxum'). *Curr Med Res Opin* 1992;12:584-93.
- Lane DA, Ireland H, Wolff S, et al.** Plasma concentrations of fibrinopeptide A, fibrinogen fragment B β 1-42 and β -thromboglobulin following total hip replacement. *Thromb Res* 1982;26:111-8.
- Langsjoen PH, Murray RA.** Cardiovascular complications of total hip replacement. *Tex Med* 1973;69:75-8.
- Lassen MR, Borris LC, Christiansen HM, et al.** Low molecular weight heparin in the prevention of thromboembolism in elective total hip replacement. *Thromb Haem* 1989;62:126.
- Lassen MR, Borris LC, Christiansen HM, et al.** Prevention of thromboembolism in 190 hip arthroplasties: comparison of LMW heparin and placebo. *Acta Orthop Scand* 1991;62:33-8.
- Lassen MR, Borris LC, Christiansen HM, et al.** Heparin/dihydroergotamine for venous thrombosis prophylaxis: comparison of low-dose heparin and low molecular weight heparin in hip surgery. *Br J Surg* 1988;75:686-9.
- *Laverick MD, Croal SA, Mollan RAB.** Orthopaedic surgeons and thromboprophylaxis. *Br Med J* 1991;303:549-50.
- Lazansky MG.** Complications revisited: the debit side of total hip replacement. *Clin Orthop* 1973;95:96-103.
- Lemos MJ, Sutton D, Hozack WJ, et al.** Pulmonary embolism in total hip and knee arthroplasty: risk factors in patients on warfarin prophylaxis and analysis of the proliferation time as an indicator of warfarin's prophylactic effect. *Clin Orthop* 1992;282:158-63.
- Levack B, Bolton AE, Cooke ED, Flanagan JP.** Salivary beta-thromboglobulin: a possible marker for deep vein thrombosis following elective hip surgery. *Thromb Res* 1986;41:319-24.
- Levine MN, Hirsh J, Gent M, et al.** Prevention of deep vein thrombosis after elective hip surgery: a randomised trial comparing low molecular weight heparin with standard unfractionated heparin. *Ann Intern Med* 1991;114:545-51.
- Levine MN, Planes A, Hirsh J, et al.** The relationship between anti-factor Xa level and clinical outcome in patients receiving enoxaparin low molecular weight heparin to prevent deep vein thrombosis after hip replacement. *Thromb Haemost* 1989;62:940-4.
- Leyvraz P, Bachmann F, Bohnet J, et al.** Thromboembolic prophylaxis in total hip replacement: a comparison between the low molecular weight heparinoid Lomoparan and heparin-dihydroergotamine. *Br J Surg* 1992;79:911-4.
- Leyvraz PF, Bachmann F, Hoek J, et al.** Prevention of deep vein thrombosis after hip replacement: randomised comparison between unfractionated heparin and low molecular weight heparin. *Br Med J* 1991;303:543-8.
- Leyvraz PF, Richard J, Bachmann F, et al.** Adjusted versus fixed-dose subcutaneous heparin in the prevention of deep-vein thrombosis after total hip replacement. *N Engl J Med* 1983;309:954-8.
- *Lowe GD, Greer IA, Cooke TG, et al.** Risk of and prophylaxis for venous thromboembolism in hospital patients: thromboembolic risk factors (THRIFT) consensus group. *Br Med J* 1992;305:567-74.

- Lubinus HH.** Total hip replacement using the 'Brunswick-system'. *Clin Orthop* 1973;95:211-2.
- McCraw JB, Furlow LT Jr.** The *dorsalis pedis* arterialized flap: a clinical study. *Plast Reconstr Surg* 1975;55:177-85.
- Mackey D, Dowling F, Sheehan J.** An evaluation of the prophylactic value of rotary beds on the incidence of deep vein thrombosis following total hip replacement. *Ir Med J* 1983;76:305-7.
- Mannucci PM, Citterio LE, Panajotopoulos N.** Low-dose heparin and deep-vein thrombosis after total hip replacement. *Thromb Haemost* 1976;36:157-64.
- Matzsch T, Bergqvist D, Fredin H, Hedner U.** Safety and efficacy of a low molecular weight heparin (Logiparin) versus dextran as prophylaxis against thrombosis after total hip replacement. *Acta Chir Scand Suppl* 1988;543:80-4.
- Matzsch T, Bergqvist D, Fredin H, Hedner U, Ostergaard P.** Influence of a low molecular weight heparin on the inhibition of factor Xa and thrombin in hip surgery. *Thromb Res* 1989;56:559-64.
- McManus F.** The incidence of deep venous thrombosis after total hip replacement using Dextran 70 prophylaxis: a venographic study. *Ir J Med Sci* 1976;145:201-6.
- ***McNally MA, McAlinden MG, O'Connell BM, Mollan RAB.** The postphlebotic syndrome five years after total hip replacement. In: *British Orthopaedic Association Conference*, 1994.
- Mendes DG.** Prophylactic treatment with dextran 70 in total hip replacement. *Clin Orthop* 1973;90:110-5.
- Menzin J, Richner R, Huse D, Colditz GA, Oster G.** Prevention of deep-vein thrombosis following total hip replacement surgery with Enoxaparin versus unfractionated heparin: a pharmacoeconomic evaluation. *Ann Pharmacother* 1994;28:271-5.
- Moczynski G, Abraham E, Barmada R, Ray RD.** Evaluation of total hip replacement arthroplasties. *Clin Orthop* 1973;95:213-6.
- Modig J, Borg T, Karlström G, Maripuu E, Sahlstedt B.** Thromboembolism after total hip replacement: role of epidural and general anaesthesia. *Anesth Analg* 1983;62:174-80.
- Modig J, Hjelmstedt Å, Sahlstedt B, Maripuu E.** Comparative influences of epidural and general anaesthesia on deep vein thrombosis and pulmonary embolism after total hip replacement. *Acta Chir Scand* 1981;147:125-30.
- Mohr DN, Silverstein MD, Ilstrup DM, Heit JA, Morrey BF.** Venous thromboembolism associated with hip and knee arthroplasty: current prophylactic practices and outcomes. *Mayo Clin Proc* 1992;67:861-70.
- ***Moore DJ, Freeman MAR.** Venous insufficiency after total hip replacement. Presented at symposium on thrombo-embolic complications following total hip replacement at the British Orthopaedic Association meeting. 1993.
- Morris GK, Henry APJ, Preston BJ.** Prevention of deep-vein thrombosis by low-dose heparin in patients undergoing total hip replacement. *Lancet* 1974;ii:797-9.
- Morris WT, Hardy AE.** The effect of dihydroergotamine and heparin on the incidence of thromboembolic complications following total hip replacement: a randomized controlled clinical trial. *Br J Surg* 1981;68:301-3.
- Moskovitz PA, Ellenberg SS, Feffer HL, et al.** Low-dose heparin for prevention of venous thromboembolism in total hip arthroplasty and surgical repair of hip fractures. *J Bone Joint Surg [Am]* 1978;60-A:1065-70.
- ***Murray WR.** Results in patients with total hip replacement arthroplasty. *Clin Orthop* 1973;95:80-90.
- Myrnel T, Larsen TS, Reikeras O.** Lipolytic effect of low-molecular-weight-heparin (Fragmin) and heparin/dihydroergotamine in thromboprophylactic doses during total hip replacement. *Scand J Clin Lab Invest* 1992;52:741-5.
- Nicholson OR.** Total hip replacement: an evaluation of the results and technics, 1967-1972. *Clin Orthop* 1973;95:217-23.
- ***NIHCC.** National Institutes of Health Consensus Conference: prevention of venous thrombosis and pulmonary embolism. *JAMA* 1986;256:744-9.
- Nillius SA, Nylander G.** Deep vein thrombosis after total hip replacement: a clinical and phlebographic study. *Br J Surg* 1979;66:324-6.
- Nillius SA, Ahlberg A, Arborelius M, Rosberg B.** Preoperative normovolaemic haemodilution with Dextran 70 as a thromboembolic prophylaxis in total hip replacement. *Int Orthop* 1979;3:197-202.
- Nilsen DW, Naess-Andresen KF, Kierulf P, et al.** Graded pressure stockings in prevention of deep vein thrombosis following total hip replacement. *Acta Chir Scand* 1984;150:531-4.
- Nilsen DW, Jeremic M, Weisert OK.** An attempt at predicting post-operative deep vein thrombosis by preoperative coagulation studies in patients undergoing total hip replacement. *Thromb Haemost* 1980;43:194-7.
- Owen TD, Moran CG, Smith SR, Pinder IM.** Results of uncemented porous-coated anatomic total hip replacement. *J Bone Joint Surg [Br]* 1994;76-B:258-62.
- Paient G, Wessinger SJ, Waltman AC, Harris WH.** Low-dose warfarin versus external pneumatic compression for prophylaxis against venous thromboembolism following total hip replacement. *J Arthroplasty* 1987;2:23-6.
- Paient G, Wessinger SJ, Waltman AC, Harris WH.** Surveillance of deep vein thrombosis in asymptomatic total hip replacement patients. *Am J Surg* 1988;155:400-4.
- Paient GD, Wessinger SJ, Hughes R, Harris WH.** Routine use of adjusted low-dose warfarin to prevent venous thromboembolism after total hip replacement. *J Bone Joint Surg [Am]* 1993;75-A:893-8.
- Paramo JA, Alfaro MJ, Rocha E.** Postoperative changes in the plasmatic levels of tissue type plasminogen activator and its fast acting inhibitor: relationship to deep vein thrombosis and influence of prophylaxis. *Thromb Haemostas* 1985;54:713-6.
- Paramo JA, Rocha E.** Deep vein thrombosis and related platelet changes after total hip replacement. *Haemostas* 1985;15:389-94.
- ***Pearson ES, Hartley HO.** *Biometrika tables for statisticians*. Vol. 1. Cambridge: Cambridge University Press, 1966:227.
- Pellegrini VD, Langhans MJ, Totterman S, Marder VJ, Francis CW.** Embolic complications of calf thrombosis following total hip arthroplasty. *J Arthroplasty* 1993;8:449-57.
- Planes A, Vochelle N, Fagola M.** Total hip replacement and deep vein thrombosis. *J Bone Joint Surg [Br]* 1990;72-B:9-13.
- Planes A, Vochelle N, Fagola M, et al.** Efficacy and safety of a perioperative Enoxaparin regimen in total hip replacement under various anaesthetics. *Am J Surg* 1991;161:525-31.
- Planes A, Vochelle N, Fagola M, et al.** Once-daily dosing of Enoxaparin (a low molecular weight heparin) in prevention of deep vein thrombosis after total hip replacement. *Acta Chir Scand Suppl* 1990;556:108-15.
- Planes A, Vochelle N, Fagola M, Feret J, Bellaud M.** Prevention of deep vein thrombosis after total hip replacement: the effect of low-molecular-weight heparin with spinal and general anaesthesia. *J Bone Joint Surg [Br]* 1991;73-B:418-22.
- Planes A, Vochelle N, Ferru J, et al.** Enoxaparin, low molecular weight heparin: its use in prevention of deep venous thrombosis following total hip replacement. *Haemostasis* 1986;16:152-8.
- Planes A, Vochelle N, Mazas F, et al.** Prevention of postoperative venous thrombosis: a randomized trial comparing unfractionated heparin with low molecular weight heparin in patients undergoing total hip replacement. *Thromb Haemost* 1988;60:407-10.
- Ritter MA, Hamilton CW.** A comparative analysis of warfarin and low-dose heparin as thromboembolism prophylaxis in total hip replacement patients. *Ann Surg* 1975;181:896-901.
- Rocha E, Alfaro MJ, Paramo JA, Canadell JM.** Preoperative identification of patients at high risk of deep venous thrombosis despite prophylaxis in total hip replacement. *Thromb Haemost* 1988;59:93-5.
- Rogers PH, Walsh PN, Marder VJ, et al.** Controlled trial of low-dose heparin and sulfipyrazone to prevent venous thromboembolism after operation on the hip. *J Bone Joint Surg [Am]* 1978;60-A:758-62.
- ***Rosendaal FR.** The emergence of a new species: the professional meta-analyst. *J Clin Epidemiol* 1994;47:1325-6.
- Rothermel JE, Wessinger JB, Stinchfield FE.** Dextran 40 and thromboembolism in total hip replacement surgery. *Arch Surg* 1973;106:135-7.
- Sagar S, Maffei FH, Stamatakis JD, et al.** Efficacy of low-dose heparin in prevention of extensive deep-vein thrombosis in patients undergoing total-hip replacement. *Lancet* 1976;i:1151-4.
- Sakai DN, Amstutz HC.** Prevention of thromboembolic phenomena. *Clin Orthop* 1976;121:108-12.
- Salvati EA, Lachiewicz P.** Thromboembolism following total hip-replacement arthroplasty: the efficacy of dextran-aspirin and dextran-warfarin in prophylaxis. *J Bone Joint Surg [Am]* 1976;58-A:921-5.

- Salvati EA, Wilson PD Jr, Jolley MN, et al.** A ten-year follow-up study of our first one hundred consecutive Charnley total hip replacements. *J Bone Joint Surg [Am]* 1981;63-A:753-67.
- ***Salzman EW, Harris WH.** Prevention of venous thromboembolism in orthopaedic patients. *J Bone Joint Surg [Am]* 1976;58-A:903-13.
- Santori FS, Vitullo A, Stopponi M, Santori N, Ghera S.** Prophylaxis against deep-vein thrombosis in total hip replacement: comparison of heparin and foot impulse pump. *J Bone Joint Surg [Br]* 1994; 76-B:579-83.
- Sautter RD, Koch EL, Myers WO, et al.** Aspirin-sulfinpyrazone in prophylaxis of deep venous thrombosis in total hip replacement. *JAMA* 1983;18:2649-54.
- Schondorf TH, Hey D.** Modified 'low-dose' heparin prophylaxis to reduce thrombosis after hip joint operations. *Thromb Res* 1978;12: 153-63.
- Seagroatt V, Tan HS, Goldacre M, et al.** Elective total hip replacement: incidence, emergency readmission rate and postoperative mortality. *Br Med J* 1991;303:1431-5.
- Sharrock NE, Brien WW, Salvati EA, et al.** The effect of intravenous fixed-dose heparin during total hip arthroplasty on the incidence of deep-vein thrombosis: a randomised, double-blind trial in patients operated on with epidural anesthesia and controlled hypotension. *J Bone Joint Surg [Am]* 1990;72-A:1456-61.
- Sharrock NE, Go G, Mineo R, Harpel PC.** The hemodynamic and fibrinolytic response to low dose epinephrine and phenylephrine infusions during total hip replacement under epidural anesthesia. *Thromb Haemost* 1992;68:436-41.
- Siegel RS, Rae JL, Ryan NL, et al.** The use of Indium-111 labelled platelet scanning for the detection of asymptomatic deep venous thrombosis in a high risk population. *Orthopedics* 1989;12:1439-43.
- Sikorski JM, Hampson WG, Staddon GE.** The natural history and aetiology of deep vein thrombosis after total hip replacement. *J Bone Joint Surg [Br]* 1981;63-B:171-7.
- Silvergleid AJ, Bernstein R, Burton DS, et al.** ASA-dipyridamole prophylaxis in elective total hip replacement. *Orthopedics* 1978;1: 19-25.
- Smith RE, Turner RJ.** Total hip replacement using methylmethacrylate cement: an analysis of data from 3482 cases. *Clin Orthop* 1973; 95:231-8.
- Soreff J, Johnsson H, Diener L, Goransson L.** Acetylsalicylic acid in a trial to diminish thromboembolic complications after elective hip surgery. *Acta Orthop Scand* 1975;46:246-55.
- Sorensen JV, Borris LC, Lassen MR, et al.** Levels of thrombin-anti-thrombin-III complex and factor VIII activity in relation to post-operative deep vein thrombosis and influence of prophylaxis with a low-molecular-weight heparin. *Blood Coagul Fibrinolysis* 1990;1: 389-92.
- Sorensen JV, Lassen MR, Borris LC, et al.** Reduction of plasma levels of prothrombin fragments 1 and 2 during thromboprophylaxis with a low-molecular-weight heparin. *Blood Coagul Fibrinolysis* 1992;3:55-9.
- Spiro TE, Johnson GJ, Christie MJ, et al.** Efficacy and safety of Enoxaparin to prevent deep venous thrombosis after hip replacement surgery. *Ann Intern Med* 1994;121:81-9.
- Stamatakis JD, Kakkar VV, Lawrence D, Bentley PG, Nairn D, Ward V.** Failure of aspirin to prevent postoperative deep vein thrombosis in patients undergoing total hip replacement. *Br Med J* 1978;ii:1031.
- Stauffer RN, Johnston RC.** Total hip replacement. *Arch Surg* 1971; 103:668-71.
- Swierstra BA, Stibbe J, Schouten HJ.** Prevention of thrombosis after hip arthroplasty: a prospective study of preoperative oral coagulants. *Acta Orthop Scand* 1988;59:139-43.
- Ten Cate JW.** Prevention of deep venous thrombosis following total hip replacement surgery by Orgaran. *Haemostasis* 1992;22:109-11.
- Thorburn J, Loudon JR, Vallance R.** Spinal and general anaesthesia in total hip replacement: frequency of deep vein thrombosis. *Br J Anaesth* 1980;52:1117-21.
- Torgerson W.** Three years of experience with total hip replacement. *Clin Orthop* 1973;95:151-7.
- Tørholm C, Broeng L, Seest Jørgensen P, et al.** Thromboprophylaxis by low-molecular-weight heparin in elective hip surgery: a placebo controlled study. *J Bone Joint Surg [Br]* 1991;73-B:434-8.
- Turpie AGC, Levine MN, Hirsh J, et al.** A randomised controlled trial of a low-molecular-weight heparin (Enoxaparin) to prevent deep venous thrombosis in patients undergoing elective hip surgery. *N Engl J Med* 1986;315:925-9.
- ***Unwin AJ, Jones JR, Harries WJ.** Current UK opinion on thromboprophylaxis in orthopaedic surgery: its use in routine total hip and knee arthroplasty. *Ann R Coll Surg Engl* 1995;77:351-4.
- Warwick D, Williams MH, Bannister GC.** Death and thromboembolic disease after total hip replacement: a series of 1162 cases with no routine chemical prophylaxis. *J Bone Joint Surg [Br]* 1995;77-B: 6-10.
- ***Warwick D, Perez J, Vickery C, Bannister G.** Does total hip arthroplasty predispose to chronic venous insufficiency? *J Arthroplasty* 1996;11(in press).
- ***Warwick D, Freeman MAR.** Overall survival rate is the most important measure. *BMJ* 1995;311:572.
- Welin-Berger T, Bygdeman S, Mebius C.** Deep vein thrombosis following hip surgery. *Acta Orthop Scand* 1982;53:937-945.
- Westermann K, Trentz O, Pretschner P, Mellmann J.** Thromboembolism after hip surgery. *Int Orthop* 1981;4:253-7.
- ***Williams MH, Frankel SJ, Nanchahal K, et al.** Total hip replacement. In: Stevens A and Raftery J, eds. *Health care needs assessment: the epidemiologically based needs assessment reviews*. Oxford: Radcliffe Medical Press, 1994:448-523.
- Wilson PD Jr, Amstutz HC, Czerniecki A, Salvati EA, Mendes DG.** Total hip replacement with fixation by acrylic cement: a preliminary study of 100 consecutive McKee-Farrar prosthetic replacements. *J Bone Joint Surg [Am]* 1972;54-A:207-36.
- Wittman PH, Wittman FW, Ring PA.** Venous thromboembolic disease in uncemented total hip replacement surgery: a one-year follow-up of 490 patients. *J R Soc Med* 1991;84:536-9.
- Woolson ST, Watt JM.** Intermittent pneumatic compression to prevent proximal deep venous thrombosis during and after total hip replacement: a progressive, randomized study of compression alone, compression and aspirin, and compression and low-dose warfarin. *J Bone Joint Surg [Am]* 1991;73-A:507-13.
- Wroblewski M, Siney PD, White R.** Fatal pulmonary embolism after total hip arthroplasty: seasonal variation. *Clin Orthop* 1992;276: 222-4.