Clinical Abstract

Potential complications associated with the implantation of endoprostheses

The risk of complication associated with both cemented and non-cemented arthroplasty is generally very low. The careful preparation of the patient prior to the procedure and conscientious surgical techniques, especially in terms of modern cementing methods can further reduce the risk of complications.

Joint replacement operations are among the most common elective surgical procedures. In 2009, nearly 2.9 million joint replacement operations were performed worldwide. These included 1.4 million hip replacements and 1.1 million knee endoprostheses implantations (1). The main indications are arthrosis, which approximately 355 million people suffer from worldwide (1) and rheumatoid arthritis (2). At the same time, joint replacement operations are among the safest surgical procedures, particularly considering the generally advanced age and thus frequently associated multimorbidity of the patients. The perioperative mortality involved with cemented total hip replacement implantation is approximately 0.06–0.09% (3–5).

As with any surgical procedure, arthroplasty-related complications can occur as well. In the overwhelming majority of these cases, there is no connection with the use of osteocementum, meaning these complications can occur both in conjunction with cemented as well as non-cemented procedures. Table 1 provides an overview of complications that can occur with any operation as well as specific endoprosthesis-related complications.

General complications	Special endoprosthesis-related complications
▪ Thrombosis and pulmonary embolism after the procedure	▪ Restricted mobility
▪ Wound healing disorders	▪ Fractures near the prosthesis
▪ Infection, swelling	▪ Instability of the prosthesis, aseptic loosening of the prosthesis
▪ Injury of blood vessels and nerves, after-bleeding and haematomas	▪ Periprosthetic infection, soft-tissue infection
▪ Anaesthesia-related complications	▪ Persistent pain
▪ Allergic reactions	▪ Bone cement implantation syndrome (BCIS)

Table 1. Possible complications involved with a joint replacement operation

Frequent complications associated with endoprosthetic operations

Venous thrombo-embolism (6, 7) is one of the most frequent complications seen in patients undergoing more serious orthopaedic surgery, such as for femoral neck fractures, knees and, in particular, total hip replacements. Without thrombosis prophylaxis, 40–80% of patients belonging to a high-risk group experience a deep leg vein thrombosis within 7–14 days; 4–10% of these patients suffer from a clinically-relevant, potentially fatal pulmonary embolism (8). Here, the risk following a total hip replacement operation is greater than for a total knee replacement operation. However, the administration of heparin and anticoagulants for thrombosis prophylaxis is still not practiced to a sufficient extent in many cases (9, 10). According to the results of a prospective Swiss study, patients undergoing knee replacements (94 %), hip replacements (81%) and fracture treatments (80 %) as well as after therapeutic arthroscopy (73 %) receive adequate thrombosis prophylaxis more often than patients who have just undergone cancer, for example (11). By far the most serious complication following implantation of an endoprosthesis is periprosthetic infection (detailed information on periprosthetic infection can be found in the Up2dates publications “Biofilm” and “The prophylactic use

of antibiotic-containing osteocementum in primary endoprosthetics"). On average, about 5 % of all surgical implants become infected (12). The infection rates in the case of endoprostheses are < 1% for total hip replacements and < 2 % for total knee replacements (13). Contamination from foreign material usually occurs perioperatively or at a later time due to the haematogenous spread of pathogens; the infections are usually biofilm-related (14, 15).

What complications associated with cementing can occur?

In conjunction with the cementing of an implant or after the blood flow occlusion is terminated, a set of symptoms referred to as bone cement implantation syndrome (BCIS) can occur (16). The clinical picture can take on very different forms. It is characterised by a drop in blood pressure, usually in combination with bradycardia, increased pressure in pulmonary circulation and a deterioration in gaseous exchange (17). The syndrome can also appear after performing cement-free anchoring of an endoprosthesis. The exact incidence is unknown. In a study of 48 patients who underwent total hip replacements, 2 % showed a drop in systolic blood pressure greater than 30 %; 17 % of patients showed a drop in oxygen saturation greater than 5 % (18).

The particularities of the aetiology and pathophysiology are not fully understood. Four main hypotheses have emerged from the scientific discussion which seek to explain the occurrence of implantation syndrome:

- **The methyl methacrylate (MMA) hypothesis:** This hypothesis is based mainly on the finding that toxic MMA monomers circulating in the blood can cause vasodilation (19). However, animal experiments performed on dogs have shown that maximum in vivo MMA concentrations found in the plasma are considerably lower than those necessary for causing pulmonary or cardiovascular effects (20, 21). Thus, the direct effect of MMA monomers on the vascular system is unlikely to be the cause of BCIS (22, 23).

- **The embolism hypothesis:** Today, researchers assume BCIS is of embolic origin. In this respect, the syndrome appears in the form of tiny fat and bone marrow particles caused by a disseminated pulmonary embolism, which is triggered by the intravascular "pressing" of the contents in the marrow cavity (Fig. 1) (23). Several findings support this hypothesis. For example, during the operation echocardiograms have shown tiny embolisms ("snow flurries") in the right region of the heart and in the pulmonary arteries. Interestingly, these mini-embolisms were seen both in patients with prosthesis using cemented and non-cemented anchoring. Studies of dogs showed comparable results showing post-operative fat and bone marrow embolisms in the lungs (22). A combination of mechanical obstruction from the pulmonary embolism and media-

Fig. 1. Blood drained on both sides at the same time from the internal iliac artery during and immediately after simultaneous cementing of both femora while asleep. When the osseous bed is flushed using a blow syringe (right side) there is a considerably greater fat supernatant – a sign of bone marrow mobilisation – than when the osseous bed is flushed using pulse lavation (left side) (23, 24).

tor-affected vascular constriction are being discussed as the cause of the hypoxia and lower oxygen saturation (26). The embolism hypothesis currently in favour is still unable to explain all phenomena of the implantation syndrome. For example, the embolisation is not always attributed to haemodynamic changes, and there is only a weak correlation between the extent of embolisation and the extent of the drop in blood pressure or hypoxia (18). Furthermore, there were no indications that MMA monomers are capable of causing embolisms and haemodynamic changes (23).

- **The anaphylaxis hypothesis:** An anaphylactic-allergic reaction was discussed as a potential cause for bone cement implantation syndrome. Hence, an increase in plasma histamine was discovered in patients who exhibited a drop in blood pressure with the endoprosthetic implantation (27). Premedicating with H1 and H2 anti-histamines made it possible to reduce the frequency of clinical effects. A complement activation with an increase of anaphylatoxins during implantation was also documented, which could potentially trigger an anaphylactic reaction (28). A small controlled, double-blind study showed that high dosages of methylprednisolone can reduce the complement activation as well as the hypoxia (29). However, more recent studies were unable to verify a complement activation (30) or increase in histamine (31, 32). Therfore this hypothesis still requires further evidence.

- **The thermal bone effects hypothesis:** During hardening of the cement, heat from an exothermic reaction is given off to the surroundings. This heat was debated as a potential cause for local coagulation and subsequent embolisation of microthrombi in the lungs (33, 34). However, there is no evidence supporting this hypothesis (35). In particular, the relatively low temperatures that are reached and the time course of the implantation syndrome are counter to the thermal hypothesis (36).

Which patients have a greater risk of complications?

Whether or not complications occur in the patient during the cemented anchoring of a joint replacement depends on several factors (Table 2). Apart from age, the preoperative clinical state of the patient is the chief determining factor. Here it is possible that cardiopulmonary concomitant diseases in particular can affect the clinical picture of the implantation syndrome (37). Therefore, one can expect to see patients with a pre-existing right ventricular dysfunction showing a greater reaction to an increase in the pulmonary-vascular resistance than patients who do not suffer from such a dysfunction (16, 38).

One other major risk factor is considered to be the presence of a malignant disease and bone metastasis. This is made clear by the results from a retrospective study (n=55) in which all three patients who had major intraoperative complications were suffering from a metastasising tumour (39). In addition, malignant diseases are often accompanied by hypercoagulability, which further promotes the development of complications. Table 2 provides an overview of patient-related risk factors for cemented endoprosthetics.

What surgery-related factors increase the risk of complications?

Aside from the patient related factors, there are also risk factors associated with the actual surgical procedure; in particular, during the intrafemoral pressure introduction phase (Fig. 2), which can increase the risk of complications and determine how the clinical picture of the implantation syndrome will appear (16). It has been possible to identify such factors in recent years (Table 3). What is clear is that implantation-associated complications occur almost exclusively with joint replacement operations of the hip. In the case of a hip replacement, the risk is especially high when long-shaft femur prostheses are used. In addition, complications occur more frequently in cases of a femoral canal that has not previously undergone surgery, i.e. in primary operations.

Finally, the cementing technique that is used plays a key role. The risk of complications increases when aspects of modern cementing methods are not taken into consideration (Table 3). Complications can be avoided, for example, by using pulse lavation to adequately flush the bone surfaces prior to cementing or by mixing the cement under vacuum conditions and using retrograde application.

Patient-related risk factors
▪ Advanced age
▪ Low physical reserves
▪ Pre-existing pulmonary hypertension
▪ Pronounced cardiac disease (NYHA* III-IV)
▪ Bone metastases
▪ Concomitant hip fractures, particularly pathological or intertrochanteric fractures
▪ Osteoporosis

* New York Heart Association classification of heart diseases (40).

Table. 2. Patient-related risk factors (16, 37).

Surgical technique-related risk factors
▪ Femoral canal that has not yet undergone surgery (primary operation)
▪ Implantation of a long-shaft prosthesis
▪ Manual application of the bone cement
▪ Insufficient flushing, e.g. using a syringe

Table 3. Surgical technique-related risk factors (16).

How can the risk of complications be minimised?

The risk of complications in terms of implantation syndrome can be reduced by taking various measures. Before the endoprosthetic restoration, particular attention should be paid to pre-existing concomitant diseases (16). From the perspective of the internists and anaesthesiologists, efforts should be made to optimise the clinical state of risk patients preoperatively in consultation with the surgeons, for example with an optimised treatment of cardiopulmonary illnesses. If necessary, a more intensive haemodynamic monitoring by inserting a pulmonary artery catheter, invasive arterial blood-pressure test and central phlebopiezometry should be considered (5, 42). The results from an animal experiment study furthermore suggest that haemodynamic embolism-associated changes can be more pronounced when using inhalation anaesthetics than, for example, intravenous fentanyl-diazepam combinatory anaesthesia (43). Forgoing use of nitrous oxide should also be considered in order to prevent more severe air embolisms that may occur.

It is also possible to reduce risks on the surgical side. First of all, the careful haemostasis should be mentioned here in addition to the selection of the appropriate femoral prosthesis, preferably with a short shaft (42). However, the focus should be on taking measures that fall under the rubric of "modern cementing techniques". These include vacuum-mixing of the bone cement in order to produce a homogeneous structure and reduce air pockets. As a result of this practice, only 11% of patients in a study of 72 high-risk patients with femoral fractures showed signs of implantation syndrome when cement was vacuum-mixed versus 53 % for whom mixing was performed under normal air pressure conditions (44). The lavation of the spongiosa and the medullary canal, preferably using a pulse lavage system, before applying the cement is also of great prophylactic importance. Sufficient flushing of the bone minimises the quantity of potential embolism-causing materials by ridding the spongiosa structures of bone marrow and small bone splinters. In addition, the pressurised pulsing and flushing minimise the release of haemodynamic and thromboembolic-active mediators (23, 35, 45, 46) (Fig. 1, 3).

Finally, the cement should not be applied manually but rather retrograde before the cement application, using a cement pistol to ventilate the area before the cement. The slow insertion of the implant, the careful application of pressure and use of a marrow cavity stopper have also proven advantageous (47). Table 4 provides an overview of the anaesthesia-relevant and surgical measures recommended to prevent the occurrence of implantation syndrome.

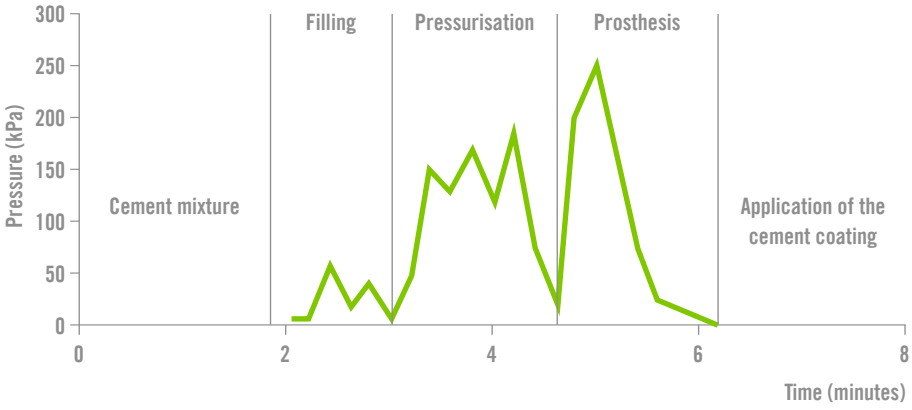

Fig. 2. Schematic illustration of the intrafemoral pressure conditions while implanting a total hip replacement prosthesis (41).

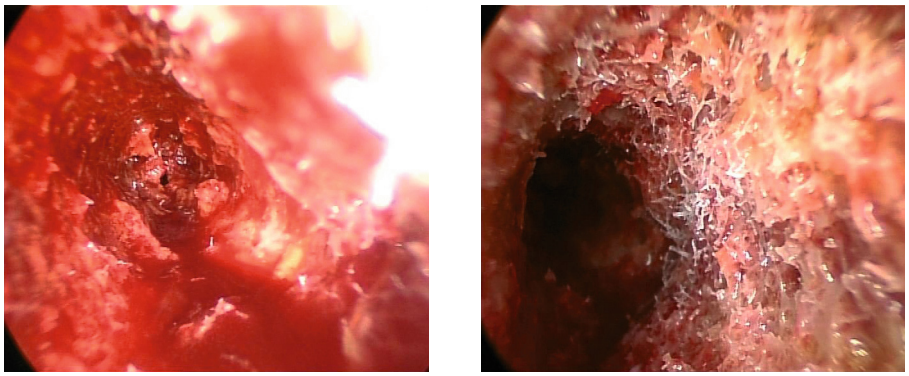

Fig. 3. Improved cementing results after using a pulse lavation system (right) compared to a non-lavaged femur (left).

Conclusion

Joint replacement operations are among the most common and also safest operations performed worldwide. A small risk of complications does exist, however. Particularly when implanting hip joint prosthesis, a temporarily reduced oxygen saturation and drop in blood pressure can occur. The most probable cause is currently assumed to be the penetration of air and fat or bone marrow pieces into the bloodstream. There is an increased risk of complications in patients with concomitant diseases, particularly those with cardiopulmonary problems or malignancies. Optimum preparation of the patient and use of surgical methods such as modern cementing techniques make it possible to considerably reduce the risk of implantation-associated complications.

As with any surgical procedure, endoprosthetic-related complications can also occur. In the overwhelming majority of these cases, there is no connection with the use of osteocementum, meaning these complications can occur both in conjunction with cemented as well as non-cemented procedures.

Anaesthesia	Surgery
▪ Optimisation of pre-existing concomitant diseases ▪ More intensive intraoperative haemodynamic monitoring ▪ Adequate intraoperative hydration and oxygenation of the patients ▪ Forgoing inhalation anaesthesia if necessary	▪ Lavation of the medullary canal ▪ Insertion of a marrow cavity stopper underneath the shaft end ▪ Good haemostasis before applying bone cement or lining with bone cement ▪ Selecting a shorter shaft for the hip prosthesis if possible ▪ Relief hole drilled distally to the tip of the prosthesis so that air can escape at the end of the cement plug, reducing the risk of an air embolism (apply vacuum if needed) ▪ Use of cement pistol and retrograde application of the bone cement ▪ Slow insertion of the implant

Table 4. Measures for reducing the risk of complications (16, 42, 47–49)

Literatur

1. The Orthopaedic Industry Annual Report. Orthoworld Inc. 2010.
2. Hart JA. Joint replacement surgery. Med J Aust 2004; 180: S27–30.
3. Coventry MB, Beckenbaugh RD, Nolan DR, Ilstrup DM. 2,012 total hip arthroplasties. A study of postoperative course and early complications. J Bone Joint Surg Am 1974; 56: 273–284.
4. Ereth MH, Weber JG, Abel MD, et al. Cemented versus noncemented total hip arthroplasty-embolism, hemodynamics, and intrapulmonary shunting. Mayo Clin Proc 1992; 67: 1066–1074.
5. Parvizi J, Holiday AD, Ereth MH, Lewallen DG. The Frank Stinchfield Award. Sudden death during primary hip arthroplasty. Clin Orthop Relat Res 1999; 369: 39–48.
6. Deitelzweig SB, McKean SC, Amin AN, Brotman DJ, Jaffer AK, Spyropoulos AC. Prevention of venous thromboembolism in the orthopedic surgery patient. Cleve Clin J Med 2008; 75 Suppl 3: S27–36.
7. Freedman KB, Brookenthal KR, Fitzgerald RH, Jr., Williams S, Lonner JH. A meta-analysis of thromboembolic prophylaxis following elective total hip arthroplasty. J Bone Joint Surg Am 2000; 82-A: 929–938.
8. Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004; 126: 338S–400S.
9. Cohen AT, Tapson VF, Bergmann JF, et al. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study. Lancet 2008; 371: 387–394.
10. Stratton MA, Anderson FA, Bussey HI, et al. Prevention of venous thromboembolism: adherence to the 1995 American College of Chest Physicians consensus guidelines for surgical patients. Arch Intern Med 2000; 160: 334–340.
11. Kalka C, Spirk D, Siebenrock KA, et al. Lack of extended venous thromboembolism prophylaxis in high-risk patients undergoing major orthopaedic or major cancer surgery. Electronic Assessment of VTE Prophylaxis in High-Risk Surgical Patients at Discharge from Swiss Hospitals (ESSENTIAL). Thromb Haemost 2009; 102: 56–61.
12. Darouiche RO. Treatment of infections associated with surgical implants. N Engl J Med 2004; 350: 1422–1429.
13. Trampuz A, Zimmerli W. Prosthetic joint infections update in diagnosis and treatment. Swiss Medical Weekly 2005; 135: 243–251.
14. Schierholz JM, Morsczeck C, Brenner N, et al. [Special aspects of implant-associated infection in orthopedic surgery. From the pathophysiology to custom-tailored prevention strategies]. Orthopade 2004; 33: 397–404.
15. Nasser S. The incidence of sepsis after total hip replacement arthroplasty. Semin Arthroplasty 1994; 5: 153–159.
16. Donaldson AJ, Thomson HE, Harper NJ, Kenny NW. Bone cement implantation syndrome. Br J Anaesth 2009; 102: 12–22.
17. Weiler-Lorentz A. Komplikationen. In: Frietsch T, Weiler-Lorentz A, eds. Anästhesie in der Traumatologie und Orthopädie. München: Urban & Fischer/Elsevier, 2009; 92–119.
18. Lafont ND, Kalonji MK, Barre J, Guillaume C, Boogaerts JG. Clinical features and echocardiography of embolism during cemented hip arthroplasty. Can J Anaesth 1997; 44: 112–117.
19. Peebles DJ, Ellis RH, Stride SD, Simpson BR. Cardiovascular effects of methylmethacrylate cement. Br Med J 1972; 1: 349–351.
20. Modig J, Busch C, Waernbaum G. Effects of graded infusions of monomethylmethacrylate on coagulation, blood lipids, respiration and circulation. An experimental study in dogs. Clin Orthop Relat Res 1975; 113: 187–197.
21. Modig J, Busch C, Olerud S, Saldeen T, Waernbaum G. Arterial hypotension and hypoxaemia during total hip replacement: the importance of thromboplastic products, fat embolism and acrylic monomers. Acta Anaesthesiol Scand 1975; 19: 28–43.
22. Orsini EC, Byrick RJ, Mullen JB, Kay JC, Waddell JP. Cardiopulmonary function and pulmonary microemboli during arthroplasty using cemented or non-cemented components. The role of intramedullary pressure. J Bone Joint Surg Am 1987; 69: 822–832.
23. Clarius M, Heisel C, Breusch SJ. Pulmonary embolism in cemented total hip arthroplasty. In: Breusch SJ, Malchau H, eds. The well-cemented total hip arthroplasty. Berlin: Springer, 2005; 320–331.
24. Breusch SJ, Lukoschek M, Schneider U, Ewerbeck V. „State of the art" der zementierten Hüftendoprothetik. Dt Ärztebl 2000; 97: A2030–2033.
25. Clarius M, Heisel C, Breusch SJ (2005) Pulmonary embolism in cemented total hip arthroplasty. In: Breusch SJ, Malchau H, eds. The well-cemented total hip arthroplasty. Berlin: Springer, 2005. ISBN 978-3-540-24197-3; Fig. 15.9 a,b auf Seite 326.
26. Krebs J, Ferguson SJ, Nuss K, et al. Plasma levels of endothelin-1 after a pulmonary embolism of bone marrow fat. Acta Anaesthesiol Scand 2007; 51: 1107–1114.
27. Tryba M, Linde I, Voshage G, Zenz M. [Histamine release and cardiovascular reactions to implantation of bone cement during total hip replacement]. Anaesthesist 1991; 40: 25–32.
28. Bengtson A, Larsson M, Gammer W, Heideman M. Anaphylatoxin release in association with methylmethacrylate fixation of hip prostheses. J Bone Joint Surg Am 1987; 69: 46–49.
29. Gammer W, Bengtson A, Heideman M. Inhibition of complement activation by high-dose corticosteroids in total hip arthroplasty. Clin Orthop Relat Res 1988; 236: 205–209.
30. Lewis RN. Some studies of the complement system during total hip replacement using bone cement under general anaesthesia. Eur J Anaesthesiol 1997; 14: 35–39.
31. Lamade WR, Friedl W, Schmid B, Meeder PJ. Bone cement implantation syndrome. A prospective randomised trial for use of antihistamine blockade. Arch Orthop Trauma Surg 1995; 114: 335–339.
32. Mitsuhata H, Saitoh J, Saitoh K, et al. Methylmethacrylate bone cement does not release histamine in patients undergoing prosthetic replacement of the femoral head. Br J Anaesth 1994; 73: 779–781.
33. Rinecker H. New clinico-pathophysiological studies on the bone cement implantation syndrome. Arch Orthop Trauma Surg 1980; 97: 263–274.
34. Frost PM. Cardiac arrest and bone cement. Br Med J 1970; 3: 524.
35. Heisel C, Clarius M, Schneider U, Breusch SJ. [Thromboembolic complications related to the use of bone cement in hip arthroplasty-pathogenesis and prophylaxis]. Z Orthop Ihre Grenzgeb 2001; 139: 221–228.
36. Breed AL. Experimental production of vascular hypotension, and bone marrow and fat embolism with methylmethacrylate cement. Traumatic hypertension of bone. Clin Orthop Relat Res 1974; 102: 227–244.
37. Pietak S, Holmes J, Matthews R, Petrasek A, Porter B. Cardiovascular collapse after femoral prosthesis surgery for acute hip fracture. Can J Anaesth 1997; 44: 198–201.
38. Koessler MJ, Pitto RP. Fat and bone marrow embolism in total hip arthroplasty. Acta Orthop Belg 2001; 67: 97–109.
39. Herrenbruck T, Erickson EW, Damron TA, Heiner J. Adverse clinical events during cemented long-stem femoral arthroplasty. Clin Orthop Relat Res 2002; 395: 154–163.
40. Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. Boston: Little, Brown & Co, 1994.
41. McCaskie A. Femoral pressurisation. In: Breusch SJ, Malchau H, eds. The well-cemented total hip arthroplasty,. Berlin: Springer, 2000; 160–163.
42. Patterson BM, Healey JH, Cornell CN, Sharrock NE. Cardiac arrest during hip arthroplasty with a cemented long-stem component. A report of seven cases. J Bone Joint Surg Am 1991; 73: 271–277.
43. Guest CB, Byrick RJ, Mazer CD, Wigglesworth DF, Mullen JB, Tong JH. Choice of anaesthetic regimen influences haemodynamic response to cemented arthroplasty. Can J Anaesth 1995; 42: 928–936.
44. Werner L. A response to ‚Sudden deaths during hip hemi-arthroplasty', Parry G, Anaesthesia 2003; 58: 922-23. Anaesthesia 2004; 59: 200.
45. Byrick RJ, Bell RS, Kay JC, Waddell JP, Mullen JB. High-volume, high-pressure pulsatile lavage during cemented arthroplasty. J Bone Joint Surg Am 1989; 71: 1331–1336.

46. Wheelwright EF, Byrick RJ, Wigglesworth DF, et al. Hypotension during cemented arthroplasty. Relationship to cardiac output and fat embolism. J Bone Joint Surg Br 1993; 75: 715–723.
47. Huo MH, Brown BS. What's new in hip arthroplasty. J Bone Joint Surg Am 2003; 85-A: 1852–1864.
48. Evans RD, Palazzo MG, Ackers JW. Air embolism during total hip replacement: comparison of two surgical techniques. Br J Anaesth 1989; 62: 243–247.
49. McCaskie AW, Barnes MR, Lin E, Harper WM, Gregg PJ. Cement pressurisation during hip replacement. J Bone Joint Surg Br 1997; 79: 379–384.

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