



Outcomes of total hip arthroplasty in pancytopenia

Dragan Radoicic¹, Zarko Dasic², Srdan Starcevic¹, Danica Radoicic¹

ABSTRACT

Objective: Pancytopenia is a hematological entity, it confronts surgeons from time to time, and the purpose was to determine the risks, difficulties and complications involved in performing total hip arthroplasty in pancytopenic patients.

Materials and methods: single centre review of 15 patients with pancytopenia, who underwent THA. 5 patients had decreased bone marrow function, 9 increased peripheral destruction, 8 of them had chronic hepatitis with liver cirrhosis (hepatitic C in 6 and B in 2 cases).

Results: 18 THA procedures, three patients had staged bilateral THA. Average age was 63.9 years. 12 women and 3 men, 14 cementless and 4 hybrid THA-s. Average intraoperative blood loss was 930 ml, average operative time 72 min.

Conclusion: THA in pancytopenia may be challenging and burdened by higher risks and costs, than in cases of some other comorbidities. THA can be safely performed, if thorough preoperative assessment is conducted, proven and safe surgical technique used and adequate postoperative restoration of hematological imbalances achieved.

Key words: Hip arthroplasty, pancytopenia, cryoprecipitate, cementless, hybrid

Introduction

Pancytopenia is a hematological entity, an abnormal depression of all the cellular elements of the blood. It ranges from mild to severe forms. Pancytopenia may be a result of decreased bone marrow production or bone marrow failure, clonal disorders of hematopoiesis, increased non-immune-mediated destruction or sequestration of blood cells, or immune-mediated destruction of blood cells [1].

Pancytopenia is a striking feature of many serious and life-threatening illnesses, ranging from simple drug-induced bone marrow hypoplasia, megaloblastic

anemia, chronic hepatitis to fatal bone marrow aplasias and leukemias, and the severity of pancytopenia and the underlying pathology determine its management and prognosis [2]. Initially, mild impairment in marrow function may go undetected and pancytopenia may become apparent strictly during times of stress or increased demand e.g., bleeding or infection [3]. In cases where total hip arthroplasty should be performed, pancytopenia makes surgical efforts more difficult and challenging.

The objectives here were to determine the risks, difficulties and complications involved in performing total hip arthroplasty (THA) in pancytopenia patients.

Materials and Methods

The research protocol was approved by the relevant institutional review board and all participants provided written informed consent.

The study was a single center retrospective review of 22 patients with pancytopenia who all underwent THA. Patients were operated on from January 2007 to July 2013. The minimum follow-up was two years (one case) with an average of 4.4 years. 26 THAs were performed in the series - 4 patients had staged bilateral THA.

In the present series, pancytopenia, with the simultaneous presence of anemia, leucopenia and thrombocytopenia, was diagnosed in the presence of anemia (hematocrit value <0.30 , hemoglobin less than 13.5g/dl in males or 11.5g/dl in females), leucopenia ($WBC < 3.0 \times 10^9/L$), or thrombocytopenia (platelets $< 100 \times 10^9/L$). Severe pancytopenia (symptomatic anemia, $WBC < 0.5 \times 10^9/L$, and platelets $< 20 \times 10^9/L$) was diagnosed in 6 cases. All operations were performed by two senior surgeons and under general anesthesia conducted by senior anesthesiologists. All patients required postoperative transfusion. In the majority of cases, platelets, fresh frozen plasma (FFP), cryoprecipitate, and albumin solutions were occasionally administered preoperatively, but more often postoperatively. Whether they were and how much FFP or cryoprecipitate were used for treating a patient with massive blood loss was guided by timely tests of coagulation, including near-patient tests. All patients were regularly, pre- and postoperatively, monitored and treated by hematology, nephrology, infectious diseases and other specialists.

Regarding the etiology of pancytopenia, 11 patients had pancytopenia because of decreased bone marrow function, 10 had pancytopenia from increased peripheral destruction, and 9 had chronic hepatitis with liver cirrhosis, with or without splenomegaly, as the cause of pancytopenia (hepatitis C in 7 and hepatitis B in 2 cases). In one case, after all possible investigations took place, pancytopenia was rated as idiopathic. 10 patients in the series were undergoing chronic hemodialysis for renal failure. Those patients required additional adjustments in LMWH and antibiotic dosages by nephrology and hematology specialists. In four cases, three were on hemodialysis and it was necessary, early postop-

eratively (on the fourth or the fifth postoperative day), to discontinue chemoprophylaxis with low molecular weight heparin (LMWH). The decision to discontinue the chemoprophylaxis was rendered, when despite appropriate restorations, considerable prolonged bleeding from the postoperative wound and adverse results of the coagulation tests (international normalized ratio (INR), activated partial thromboplastin time (APTT) and platelet count) were noted. None of those patients, although without chemoprophylaxis, had deep venous thrombosis or venous thromboembolism-related complications.

With regards to the orthopedic indication for THA, 12 patients had THA for femoral neck fracture, and two had staged bilateral THA for bilateral femoral neck fracture (Figure 1 and Figure 2). 9 patients had elective procedures, and 6 of those patients had femoral head avascular necrosis (one case, bilateral staged THA) and 3 had hip arthritis as an indication for THA (one case being bilateral THA).

When it came to implants, THAs were performed as uncemented, cemented and hybridized (cementless acetabulum and cemented femoral stem). Implants used in the study were: Depuy cementless Corail hip system with Duraloc or Pinnacle acetabular cups (Depuy Warsaw, Indiana, US), Zimmer cementless Versys and M/L taper stems (Zimmer Warsaw, Indiana, US). For hybrid cases, cemented Advocate stems combined with Zimmer Trilogy acetabular cups were employed. In all situations, metal on polyethylene couplings and 28mm femoral head diameters were used. In all pancytopenia cases of cemented or hybrid THA (Figure 3), commercially available antibiotic loaded cement (Re-fobacin bone cement, Biomet Warsaw, Indiana, US). In



Figure 1. Bilateral femoral neck fracture in a pancytopenic 30-year-old female on long-term hemodialysis.

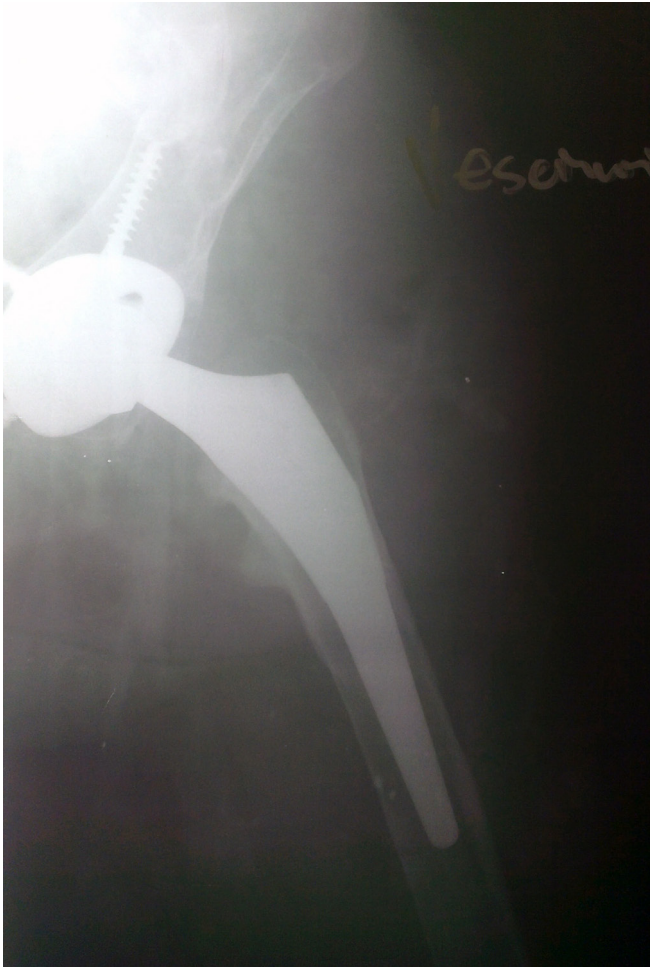


Figure 2. Uncemented left THA in a pancytopenic 30-year-old female on hemodialysis.

each case, preoperative templating was performed for the uncemented and cemented options, and the definitive decision on type of THA was made intraoperatively, primarily on the basis of bone quality.

Patients received preoperative antibiotic prophylaxis with ceftriaxone or ceftazidim 2g i.v., and in cases with allergic reactions to penicillin, gentamycin 120 mg i.v. was used. The same antibiotic regimen was conducted for at least 4 days postoperatively. In two cases with leucopenia as major feature of pancytopenia, and for two patients who regularly received immunosuppressants, after discontinuation of i.v. antibiotics, oral administration of azithromycin 250mg twice a day for 5 days (as prescribed by hematology and infective diseases specialists) took place. Suction drains were utilized in 8 THA procedures, and in 3 cases, drains were removed on the first postoperative day, in two cases on the second, and in three cases, as a consequence of excessive wound drainage, on the fourth postoperative day. All patients were treated with low molecular weight



Figure 3. Hybrid THA, for femoral neck fracture, in a 66-year-old female where antibiotic loaded cement was used for femoral stem fixation.

heparins monitored by hematology specialists (enoxaparin sodium in all cases), and chemoprophylaxis was begun preoperatively for patients with hip fractures and postoperatively for patients in the elective THA group.

Results

There were 26 THA procedures, as 4 patients had bilateral THA (in a staged procedure). The average age of the patients was 49.5 years. There were 16 women and 6 men. In terms of THAs, 16 were cementless, 4 cemented and 4 hybridized. Average intraoperative blood loss was 873 ml and the average operative time was 63 min. The mean red blood cell transfusion volume was 1710 ml (range 860 – 4400 ml). In two cases, massive blood transfusions, defined as replacement of the patients total blood volume in less than 24 hours with stored blood [4], were performed. The average wound

drainage was 630 ml (240 to 2120 ml). The average postoperative length of hospitalization was 12.9 days. Prophylactic platelets were administered in 6 cases. In 17 THA procedures, platelets were administered postoperatively. FFP at a dose of 10 to 15 ml/kg was applied in almost all cases postoperatively, and in some cases, up to 8 FFP units were administered. Cryoprecipitates were provided in 5 cases when low fibrinogen levels < 1.0 g/l were detected.

Intraoperative cell salvage with a double suction setup was employed in three cases, the patients being selected in consultation with the attending anesthesiologist. Hemostatic agents for intraoperative topical application (in most cases, oxidized regenerated methylcellulose products) were utilized in 5 cases. Immediately postoperatively, patients were transferred to an intensive care unit (ICU) and the average time spent in the ICU was 1.8 days.

Besides hematologic imbalances, other major complications were noted. One cardiac arrest (fourth postoperative day - patient recovered), three hepatic decompensations, three renal failures (two were reversible, one required dialysis), three pulmonary embolisms (two of those patients had cemented THA and one hybrid THA), and two cerebrovascular ischemic events (strokes that required neurological examination and treatment) were seen with this series. One patient with uncemented THA had early postoperative infection, *Klebsiella* sp. was isolated in cultures obtained during the revision procedure. Two stage revision with an articulating hip spacer was applied (Figure 4). One patient, a 71-year-old female (cemented THA) developed infection 12 weeks postoperatively, as *Staphylococcus aureus* was isolated in cultures, and so i.v. antibiotic therapy, under the auspices of an infectious disease specialist, was started. As a result of comorbidities and unstable medical condition, surgery was delayed and the patient subsequently developed sepsis and multiorgan failure, expiring 18 weeks postoperatively. The mortality rate was 13.63% (three patients). Besides the aforementioned mentioned patient, during follow-up, of the two other patients that died, 2.1 and 4.6 years after THA surgery, one, besides blood loss, had a cerebrovascular ischemic event postoperatively, but completely recovered in the first 6 months postoperatively.



Figure 4. An articulating hip spacer in a two-stage revision of an infected uncemented THA.

The other patient that expired had no THA complications. It was determined that the cause of death in either of these latter two cases could not be directly related to the THA procedure.

Late complications were involved in 6 cases (27.27%). In one patient, this was because of recurrent dislocations requiring revision surgery and a constrained acetabulum was used, one patient experienced periprosthetic femoral fracture, and five prosthetic loosensings were noted (two septic and three aseptic). In total, 7 patients (31.18%) required revision surgery.

Discussion

There are not many studies that have dealt with the performance and safety of THA in pancytopenic patients, and so the data regarding this topic are very limited. According to incidence of complications in this

series compared to the general population undergoing THA [5], risks of non-implant-related major complications, like blood loss, higher transfusion requirements, cardiac, hepatic and renal decompensation, pulmonary embolism, and infection, are considerably higher in pancytopenia patients than in the typical patients.

Most of the patients in this study had cirrhosis-induced peripheral destruction as a cause of pancytopenia, and Cohen et al. [6] have shown that patients undergoing total joint arthroplasty procedures are at greater risk for complications and mortality than patients without cirrhosis, the risks being even higher if trauma is an indication for THA.

A number of the patients here with femoral neck fracture, femoral head AVN, or hip arthritis were on a chronic hemodialysis regimen. Surgical treatment of hip fractures in patients with end-stage renal disease who are on chronic hemodialysis is associated with frequent complications and a high mortality rate [7]. In the series presented here, THA was opted for, but opinions in the literature are somewhat divided. Karaeminogullari et al. [7] recommended that displaced femoral neck fractures should be treated with hemiarthroplasty, while Sakalkale et al. [8] advocated THA in dialysis patients, noting however that THA should be reserved for those among this group expected to have a better life expectancy. From a similar point of view, total hip arthroplasty is best reserved for patients expecting a renal transplant or preferably for those who have already received a successful transplant according to Lieberman et al. [9].

In considering choice of implants, most of these patients received cementless THA. Li et al. [10] have shown promising medium-term results of uncemented THA in patients undergoing long-term hemodialysis, and Nagoya et al. [11], in a series of cementless THA for patients on long-term hemodialysis, confirmed that predictable long-term stability of the bone-implant interface can be achieved by cementless fixation with an extensively coated implant.

Postoperative treatment requires intensive monitoring, regular lab analysis, and close cooperation with hematology and transfusion specialists. Standard-setting groups in both the U.S [12] and England [13] have recommended a $10 \times 10^9/L$ for prophylactic platelet

transfusion trigger for all patients chronically thrombocytopenic based on chemotherapy, bone marrow transplantation, or for marrow conditions resulting in thrombocytopenia, such as aplasia or myelodysplasia. In the present series, in order to minimize the risk of major hemorrhage, after consultations with anesthesiology and hematology specialists, $20 \times 10^9/L$ was used as a threshold for prophylactic platelets. The indications for transfusing FFP, cryoprecipitate, and cryosupernatant plasma are limited. In cases of liver disease, FFP is advocated by some for the prevention of bleeding and a prolonged prothrombin time, although the response may be unpredictable and complete normalization of the hemostatic defect does not always occur. If FFP is given, coagulation tests should be repeated post-infusion to guide decision making [14,15].

In this study, intraoperative cell salvage was applied in a number of cases. General indications for cell salvage in orthopedics are major spine surgery, bilateral knee replacement, and hip and knee revisions [16]. As some of the relative contraindications include use of clotting agents, presence of bone chips, and methymetacrylate [16], there are still controversies regarding higher incidence of complications. Here, it was observed that cell salvage use in pancytopenic THA limited, applicable in a few selected cases.

Several important recommendations in pre, peri and postoperative management of pancytopenic patients undergoing THA, should be highlighted. The preoperative evaluation should focus on identification of pancytopenia cause and type, comorbidity assessment, and risk reduction. Attending surgeon and anesthesiologists should not hesitate to order multiple consultations (hematology, hepatology, nephrology, transfusiology, infectious diseases, and other specialists), pre- and postoperatively. Hepatic or renal failure, pulmonary embolism, or even cerebrovascular events, are to be anticipated. Timely interventions by hematology, hepatology, or nephrology specialists may be crucial in risk reduction and complication prevention and treatment. Discussing each case with an anesthesiologist can be of extreme importance in identifying the complex perioperative surgical, anesthetic, hemodynamic, and hemostasis issues that may be unique to pancytopenic patients.

Prior to surgery, the surgeon must arrange postop-

erative monitoring and treatment in an intensive care unit setting. Postoperative care should also be multidisciplinary. Monitoring should focus on hemostasis complications, and hepatic and renal decompensation.

The study was limited by its retrospective nature and lack of a control group.

Conclusion

Total hip arthroplasty in cases of pancytopenia may be challenging and burdened by higher risks than in cases with other comorbidities. THA in pancytopenia settings can be safely performed if thorough preoperative assessment is conducted, proven and safe surgical and anaesthesiological approaches used, and subsequent adequate postoperative restoration of hematological imbalance is ensured.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Wintrobe, Maxwell Myer. Wintrobe's clinical hematology. John P. Greer (ed). Lippincott Williams & Wilkins, Philadelphia, 2009;80-2.
2. Gayathri BN, Rao KS. Pancytopenia: A clinico hematological study. *J Lab Physicians* 2011;3:15.
3. Makheja KD, Maheshwari BK, Arain S, Kumar S, Kumari S. The common causes leading to pancytopenia in patients presenting to tertiary care hospital. *Pak J Med Sci* 2013;29:1108.
4. Klein HG, Anstee DJ. Mollison's Blood Transfusion in Clinical Medicine 11th ed. Wiley-Blackwell, Malden, Massachusetts, 2005.
5. deVries LM, Sturkenboom MC, Verhaar JA, Kingma JH, Stricker BH. Complications after hip arthroplasty and the association with hospital procedure volume: A nationwide retrospective cohort study on 50,080 total hip replacements with a follow-up of 3 months after surgery. *Acta orthopaedica* 2011;82:545-52.
6. Cohen SM, Te HS, Levitsky J. Operative risk of total hip and knee arthroplasty in cirrhotic patients. *J Arthroplasty* 2005;20:460-6.
7. Karaeminogullari O, Demirors H, Sahin O, Ozalay M, Ozdemir N, Tandogan RN. Analysis of outcomes for surgically treated hip fractures in patients undergoing chronic hemodialysis. *J Bone Joint Surg Am* 2007;89:324-31.
8. Sakalkale DP, Hozack WJ, Rothman RH. Total hip arthroplasty in patients on long-term renal dialysis. *J Arthroplasty* 1999;14:571-5.
9. Lieberman Jay R, Marc D. Fuchs, Steven B. Haas, Kevin L. Garvin, Leonard Goldstock, Ranjan Gupta, et al. Hip arthroplasty in patients with chronic renal failure. *J Arthroplasty* 1995;10:191-5.
10. Li WC, Shih CH, Ueng SW, Shih HN, Lee MS, Hsieh PH. Uncemented total hip arthroplasty in chronic hemodialysis patients: 20 hips reviewed after 2–13 years. *Acta orthopaedica* 2010;81:178-82.
11. Nagoya S, Nagao M, Takada J, Kuwabara H, Kaya M, Yamashita T. Efficacy of cementless total hip arthroplasty in patients on long-term hemodialysis. *J Arthroplasty* 2005;20:66-71.
12. Schiffer CA, Anderson KC, Bennett CL, Bernstein S, Elting LS, Goldsmith M, et al. Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology. *J Clin Oncol* 2001;19:1519-38.
13. British Committee for Standards in Haematology, Blood Transfusion Task Force (Chairman P Kelsey). Guidelines for the use of platelet transfusions. *Br J Haematol* 2003;122:10-23.
14. O'shaughnessy DF, Atterbury C, Bolton Maggs P, Murphy M, Thomas D, Yates S, et al. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. *Br J Haematol* 2004;126:11-28.
15. Schofield WN, Rubin GL, Dean MG. Appropriateness of platelet, fresh frozen plasma and cryoprecipitate transfusion in New South Wales public hospitals. *Med J Aust* 2003;178:117-21.
16. Esper SA, Waters JH. Intra-operative cell salvage: a fresh look at the indications and contraindications. *Blood Transfusion* 2011;9:139.