Preoperative hematocrit on early prosthetic joint infection and deep venous thrombosis rates in primary total hip arthroplasty: A database study

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ABSTRACT

Background: Total hip arthroplasty (THA) is a very successful surgery in restoring a patient's quality of life. Infection is a devastating complication of THA. Many risks factors for infection in THA have been identified but little is known of the effect by preoperative hematocrit.

Purpose: We aimed to evaluate the effect of preoperative hematocrit on early superficial site infections, deep infections, and deep organ space infections.

Methods: Our study cohort included patients undergoing a THA in the ACS National Surgical Quality Improvement Program database from 2006 to 2015. We conducted a multivariate logistic regression analysis to evaluate an association between preoperative hematocrit and infection controlling for patients demographics and known risk factors.

Results: A total of 98,869 patients were identified in this study. Of these, 702 (0.71%) developed a superficial site infection, 314 (0.32%) a deep infection, and 226 (0.23%) an organ space infection. Our results suggested a significant increased risk of deep infection (OR=2.38, $p=0.0120$) and organ space infection (OR=3.05, $p=0.0234$) in patients with lower preoperative hematocrit (<41). In addition, patients with lower preoperative hematocrit had higher chance to receive postoperative transfusion (OR=2.93, $p<0.0001$). However, no significant associations between preoperative hematocrit and superficial site infections ($p=0.8554$), wound dehiscence ($p=0.0660$) and DVT ($p=0.9236$) were detected.

Conclusion: Low preoperative hematocrit is associated with increased risk of deep, organ space infections, and postoperative transfusion in THA, but not with superficial site infections, wound dehiscence and DVT.

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1. Background

Total hip arthroplasty (THA) is one of the most successful surgeries and can help alleviate pain in patients with severe hip osteoarthritis. The need for THA will continue to increase as the population ages. The geriatric population in America numbered greater than 38.9 million in 2008, and it will represent 20% of the US population by 2020.²³ With the increasing elderly population, total hip arthroplasty is expected to increase by 175% over the next 25 years.² Despite patient satisfaction with THA, the procedure has

several complications including infection, instability, loosening and periprosthetic fracture.²¹

Infection is a relatively rare but devastating complication of THA for both patients and surgeons. Infection rates in total hip arthroplasty range anywhere from 1.4% to 4.4% for surgical site infections with deep infection ranging from 0.4% to 2.2%.¹⁰ There are many risk factors associated with an increased risk of infection following THA, including age, male gender, obesity, lower socioeconomic status, lack of antibiotic prophylaxis and skin preparation, metal on metal hips, bilateral procedures, history of methicillin resistant staphylococcus aureus colonization (MRSA), and prolonged hospital stay.^{5,12,13,16,20,22,24,25} The costs associated with total hip arthroplasty revision from previous infection are estimated to be around 3.6 times the cost of a primary total hip arthroplasty.⁹

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There is limited evidence on the relationship of preoperative hematocrit and infection in THA.^{4,7,18} The purpose of this study was to assess any increased risk of early infection in patients undergoing THA with lower preoperative hematocrit. We hypothesized that lower preoperative hematocrit would predispose a patient undergoing THA to infection, and lead to increased infection rates.

2. Methods and materials

The ACS National Surgical Quality Improvement Program (ACS NSQIP) database from 2006 to 2015 was queried in this study. Institutional review board (IRB) approval was not required in this study because ACS NSQIP is a de identified patient database and this study was exempt from IRB. Patients with THA in the database were identified using the CPT code 27130, and their 30 day outcomes following THA were analyzed. Exclusion criteria including patients with operative times less than 25 min or greater than 280 min, missing preoperative hematocrit values, and BMI <17.

Infection rates were calculated from the available data for all years, including superficial site infections, deep infections, and organ space infections, as defined by the NSQIP database. Organ space infection (OSI) is defined by NSQIP as an infection that involves any part of the anatomy other than the incision that was opened or manipulated during an operation. If a deep infection, for instance an abscess, were to occur anywhere besides the operative hip, then it was considered an OSI. The NSQIP database defines a deep infection as an infection that involves any tissues beneath the skin (e.g., immediate subcutaneous fat, fascial, and muscle layers) that was involved in the surgical exposure.¹⁷ A superficial site infection (SSI) is defined as incisional involvement of skin alone or involvement of subcutaneous tissue.¹¹ All of these must have occurred within the first 30 days following a procedure.

Patient demographics, preoperative comorbidities and operative variables including age, gender, obesity, steroid intake, smoking status, operative time, and diabetes status were used in the analysis, as these variables have been consistently associated with infection and DVT rates after joint replacement as evident from previous studies.^{5,12,13,16,20,22,24,25} Patient demographics and studied variables were summarized as frequency (proportion) for categorical variables and mean $\pm$ standard deviation (SD) for continuous variables. Patients were divided into two groups based on their preoperative hematocrit levels, i.e., lower group in which patients' preoperative hematocrit levels were less than 41 and higher group in which patients' preoperative hematocrit levels

were equal to higher than 41, where 41 was the median value of all patients. The comparison between two groups were conducted using *t*-test or Chi square test where appropriate. The adjusted associations between preoperative hematocrit levels and infections were evaluated using multivariable logistic regression controlling for aforementioned patients' demographics and studied variables. Adjusted odds ratio (OR) was used to indicate the association. All statistical analysis was performed using SAS software (version 9.4; SAS Institute, Cary, North Carolina). The level of significance for all analysis was set at $p < 0.05$.

3. Results

We identified 98,869 patients with THA from ACS NSQIP database after excluding criteria was met, including 44,003 (44.5%) men and 54,788 (55.5%) women. Gender information was missing in 78. On average, the identified patients were 65.0 ± 11.8 years old at the time of THA, with a mean BMI of 30.0 ± 6.3 . The average time of surgery was 93.3 ± 36.3 min. At the time of the surgery, 3746 (3.8%) patients were on steroids, and 11,534 (11.7%) patients were on medicine for diabetes. Smoking was present in 13,290 (13.4%) patients. The average hematocrit of patients going into surgery was 40.7 ± 4.3 vol% (Table 1). Compared to patients in higher preoperative hematocrit group, patients in lower preoperative hematocrit group had fewer males (27.5% vs 61.4%, $p < 0.0001$), smaller BMI (29.5 ± 6.5 vs 30.6 ± 6.0 , $p < 0.0001$), more steroid users (5.0% vs 2.6%, $p < 0.0001$), more diabetes (13.6% vs 9.7%, $p < 0.0001$) and fewer smokers (11.1% vs 15.8%, $p < 0.0001$) with similar surgical time (93.4 ± 36.9 vs 93.3 ± 35.6 , $p = 0.7599$) (Table 1).

Of the 98,869 cases, there were 702 (0.71%) superficial infections, 314 (0.32%) deep infections, and 226 (0.23%) organ space surgical site infections, 112 (0.11%) wound dehiscence, and 427 (0.43%) DVT. There were 11,212 cases (11.3%) that required postoperative transfusions. Compared to patients in higher preoperative hematocrit group, patients in lower preoperative hematocrit group had higher risks of deep infections (0.36% vs 0.27%, $p = 0.0112$), organ space infection (0.28% vs 0.18%, $p = 0.0019$), wound dehiscence (0.14% vs 0.09%, $p = 0.0215$), and postoperative transfusion (17.7% vs 5.0%, $p < 0.0001$). There was no significant differences regarding superficial site infections ($p = 0.2895$) and DVT ($p = 0.2406$) (Table 1).

A multivariate logistic regression was carried out to evaluate the adjusted effect of preoperative hematocrit on superficial, deep, organ space infection, wound dehiscence, DVT, and postoperative transfusion, controlling for sex, age, BMI, operative time, diabetes,

Table 1
Descriptive statistics of study cohort.

Variables	Mean $\pm$ SD or frequency (proportion)			P values
	Overall	hematocrit <41	hematocrit $\geq$ 41	
N	98,869	49,296 (49.9%)	49,573 (50.1%)	
Males	44,003 (44.5%)	13,553 (27.5%)	30,450 (61.4%)	<0.0001
Age at THA	65.0 ± 11.8	66.7 ± 11.2	63.4 ± 11.2	<0.0001
Surgical time (minutes)	93.3 ± 36.3	93.4 ± 36.9	93.3 ± 35.6	0.7599
BMI (kg/m ²)	30.0 ± 6.3	29.5 ± 6.5	30.6 ± 6.0	<0.0001
Steroid use	3746 (3.8%)	2443 (5.0%)	1303 (2.6%)	<0.0001
Diabetics	11,534 (11.7%)	6717 (13.6%)	4817 (9.7%)	<0.0001
Smokers	13,290 (13.4%)	5478 (11.1%)	7812 (15.8%)	<0.0001
Preoperative hematocrit (vol%)	40.7 ± 4.3	37.4 ± 3.2	44.0 ± 2.4	<0.0001
Superficial site infections	702 (0.71%)	364 (0.74%)	338 (0.68%)	0.2895
Deep infection	314 (0.32%)	179 (0.36%)	135 (0.27%)	0.0112
Organ space infection	226 (0.23%)	136 (0.28%)	90 (0.18%)	0.0019
Wound dehiscence	112 (0.11%)	68 (0.14%)	44 (0.09%)	0.0215
Postoperative Transfusion	11,212 (11.3%)	8736 (17.7%)	2476 (5.0%)	<0.0001
DVT	427 (0.43%)	225 (0.46%)	202 (0.41%)	0.2406

Table 2

Adjusted association between preoperative hematocrit and early infection and wound dehiscence in THA patients.

Complications	Adjusted OR (95%CI) ^a hematocrit <41 vs hematocrit ≥41	P values
Superficial site infections	1.04 (0.69, 1.57)	0.8554
Deep infection	2.38 (1.21, 4.69)	0.0120
Organ space infection	3.05 (1.16, 7.98)	0.0234
Wound dehiscence	3.47 (0.92, 13.03)	0.0660
DVT	0.98 (0.58, 1.65)	0.9236
Postoperative Transfusion	2.93 (2.55, 3.36)	<0.0001

^a Adjusted for patients' age, gender, BMI, steroid intake, smoking status, operative time, and diabetes status.

steroid use, and smoking status. Our results suggested increased adjusted risks of deep infection ($p=0.0120$), organ space infection ($p=0.0234$), and postoperative transfusion ($p<0.0001$) for patients with lower preoperative hematocrit level. Specifically, the adjusted odds of deep infection for patients in lower preoperative hematocrit group was 2.38 (confidence interval [CI] 1.21, 4.69) times of the odds for patients in higher group; the adjusted odds of organ space infection for patients in lower preoperative hematocrit group was 3.05 (CI 1.16, 7.98) times of the odds for patients in higher group; and the adjusted odds of receiving postoperative transfusion for patients in lower preoperative hematocrit group was 2.93 (CI 2.55, 3.36) times of the odds for patients in higher group. Our results also suggested a marginal significant adjusted association between wound dehiscence and preoperative hematocrit levels (adjusted OR=3.47, $p=0.0660$). However, there was no significant group differences for superficial site infection and preoperative hematocrit levels (adjusted OR=1.04, $p=0.8554$) and DVT ($p=0.9236$) (Table 2). Similar associations were also found from the similar multivariate logistic regressions using continuous preoperative hematocrit values (data not shown).

4. Discussion

Infection is a devastating complication of THA, one that sets the patient back and adds significant costs to the healthcare system.⁹ In this study we sought to analyze the most recent data from the NSQIP database to evaluate a possible relationship between low preoperative hematocrit and infection in THA. We hypothesized that lower preoperative hematocrit would increase the risk of infection in patients undergoing THA. Our results suggested a significant increased risk of deep infection and organ space infection in patients with lower preoperative hematocrit. In addition, patients with lower preoperative hematocrit had higher chance to receive postoperative transfusion. We found more steroid users and diabetic patients in the lower hematocrit group. Concurrently, there were less males, smaller BMI, and fewer smokers in the low hematocrit group. Chronic steroid use, high BMI, smoking are associated with higher risk of infection.^{4,5,12} We found no significant associations between preoperative hematocrit and superficial site infections, wound dehiscence and DVT were detected.

Bierbaum et al. evaluated 9482 patients from 330 surgeons across the United States undergoing total joint arthroplasty. They found the risk of infection was increased in patients requiring transfusion following TJA.³ Pruzansky et al. evaluated surgical site infection risk factors following THA or TKA in 300 patients at a single institution. Overall, 29% of the patients studied had preoperative anemia, with 49% of those anemic patients having surgical site infections.¹⁸ Greenky et al. identified 15,722 patients undergoing total joint replacement. They found a higher rate of prosthetic joint infection in patients with preoperative anemia (4.3%) than in non-anemic patients (2%).⁷ Myers et al. prospectively analyzed 225 patients undergoing THA with preoperative

anemia and found an increased risk of respiratory tract and urinary tract infections, but did not evaluate for surgical site or deep infections.¹⁴ Bozic et al. evaluated the Medicare claims database for risk factors for infection in Medicare patients and found an increased risk of surgical site infection in patients with preoperative anemia (HR=1.36).⁴ Our results are in agreement with these studies regarding risk of infection following surgery, especially in preoperative anemia versus non-anemic.

There seems to be a dichotomy of information regarding the subject of anemia, blood transfusions, and infection in patients undergoing total hip arthroplasty. As previously stated, the literature⁸ shows increased infection rates following blood transfusion, but is mixed about preoperative hematocrit. Our study showed no association with superficial surgical site infection, but it did show an increase in deep or organ space infections in patients undergoing THA who had a preoperative hematocrit <41. Low preoperative hematocrit, specifically <41, may represent a concurrent medical pathology or nutritional status of a patient. As there is an increase in infection with low preoperative hematocrit, it may be prudent to delay surgery in order to improve a patient's hematocrit. Surgeons may wish to consider referral to the patient's primary care physician or consider adding an iron supplement or erythropoietin to help promote the patient's capacity to restore blood stores prior to surgery.⁶ Not only may this help to decrease infection, but it may also decrease the need for postoperative transfusions^{1,15} which has also been associated as a risk factor for infection.^{8,19} Of course, low preoperative hematocrit could simply be a surrogate for the need for intraoperative transfusion. If it is the transfusion itself that is the cause of increased infection, then the preoperative hemodynamic state is simply a predictive marker for the need for transfusion in the future. Likewise, it is possible that the transfusion itself is only a consequence of the preoperative hematocrit, which is the main cause of concern for postoperative infection. More research regarding this topic should be undertaken to better ascertain the etiology.

Limitation of this study is that the data used in the analysis only contains information on the first thirty days post operatively. Thus, conceivably complications sustained after day 30 were missed in this study. Secondly, multivariate analysis to eliminate bias was used to control for major variables such as BMI, age, sex, smoking, diabetes, steroids but there are certainly other minor or unproven risk factors for infection which we could not account for or been able to control due to nature of database.

Finally, in clinical practice it is impossible to operate on every patients with hematocrit of greater than 41. We run the different analyses with hematocrit level as continuous and dichotomized values; and generated similar results. We only reported results with hematocrit level as dichotomized values because the resulted odds ratios were more interpretable.

In conclusion, our study using the NSQIP database suggests that lower preoperative hematocrit is associated with higher rates of deep infections and organ space infection. This information can be

used to further the field of joint arthroplasty and to help minimize the complication of periprosthetic infection in the future.

Conflict of interest

None.

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References

- Auerbach M, Goodnough LT, Picard D, Maniatis A. The role of intravenous iron in anemia management and transfusion avoidance. *Transfusion (Paris)*. 2008;48(5):988–1000.
- Bashinskaya B, Zimmerman RM, Walcott BP, Antoci V. Arthroplasty utilization in the United States is predicted by age-specific population groups. *ISRN Orthop*. 2012;2012.
- Bierbaum BE, Callaghan JJ, Galante JO, Rubash HE, Tooms RE, Welch RB. An analysis of blood management in patients having a total hip or knee arthroplasty. *J Bone Jt Surg Am*. 1999;81(1):2–10.
- Bozic KJ, Lau E, Kurtz S, et al. Patient-related risk factors for periprosthetic joint infection and postoperative mortality following total hip arthroplasty in medicare patients. *J Bone Jt Surg Am*. 2012;94(May (9)):794–800.
- Cordero-Ampuero J, de Dios M. What are the risk factors for infection in hemiarthroplasties and total hip arthroplasties? *Clin Orthop Relat Res*. 2010;468(December (12)):3268–3277.
- Feagan BG, Wong CJ, Kirkley A, et al. Erythropoietin with iron supplementation to prevent allogeneic blood transfusion in total hip joint arthroplasty: a randomized, controlled trial. *Ann Intern Med*. 2000;133(11):845–854.
- Greenky M, Gandhi K, Pulido L, Restrepo C, Parvizi J. Preoperative anemia in total joint arthroplasty: is it associated with periprosthetic joint infection? *Clin Orthop Relat Res*. 2012;470(October (10)):2695–2701.
- Innerhofer P, Klingler A, Klimmer C, Fries D, Nussbaumer W. Risk for postoperative infection after transfusion of white blood cell–filtered allogeneic or autologous blood components in orthopedic patients undergoing primary arthroplasty. *Transfusion (Paris)*. 2005;45(1):103–110.
- Klouché S, Soriali E, Mamoudy P. Total hip arthroplasty revision due to infection: a cost analysis approach. *Orthop Traumatol Surg Res*. 2010;96(2):124–132.
- Lindeque B, Hartman Z, Noshchenko A, Cruse M. Infection after primary total hip arthroplasty. *Orthopedics*. 2014;37(April (4)):257–265.
- Malone DL, Genuit T, Tracy JK, Gannon C, Napolitano LM. Surgical site infections: reanalysis of risk factors. *J Surg Res*. 2002;103(1):89–95.
- Maoz G, Phillips M, Bosco J, et al. The Otto Aufranc Award: modifiable versus nonmodifiable risk factors for infection after arthroplasty. *Clin Orthop Relat Res*. 2015;473(February (2)):453–459.
- Mraovic B, Suh D, Jacovides C, Parivizi J. Perioperative hyperglycemia and postoperative infection after lower limb arthroplasty. *J Diabetes Sci Technol*. 2011;5(March (2)):412–418.
- Myers E, O'Grady P, Dolan AM. The influence of preclinical anaemia on outcome following total hip replacement. *Arch Orthop Trauma Surg*. 2004;124(December (10)):699–701.
- Na HS, Shin SY, Hwang JY, Jeon YT, Kim CS, Do SH. Effects of intravenous iron combined with low-dose recombinant human erythropoietin on transfusion requirements in iron-deficient patients undergoing bilateral total knee replacement arthroplasty (CME). *Transfusion (Paris)*. 2011;51(1):118–124.
- Ong KL, Kurtz SM, Lau E, Bozic KJ, Berry DJ, Parvizi J. Prosthetic joint infection risk after total hip arthroplasty in the Medicare population. *J Arthroplasty*. 2009;24(September (Suppl. 6)):105–109.
- Parikh JA, Beane JD, Kilbane EM, Milgrom DP, Pitt HA. Is American College of Surgeons NSQIP organ space infection a surrogate for pancreatic fistula? *J Am Coll Surg*. 2014;219(6):1111–1116.
- Pruzansky JS, Bronson MJ, Grelsamer RP, Strauss E, Moucha CS. Prevalence of modifiable surgical site infection risk factors in hip and knee joint arthroplasty patients at an urban academic hospital. *J Arthroplasty*. 2014;29(2):272–276.
- Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic joint infection: the incidence, timing, and predisposing factors. *Clin Orthop*. 2008;466(7):1710–1715.
- Ridgeway S, Wilson J, Charlet A, Katafox G, Pearson A, Coello R. Infection of the surgical site after arthroplasty of the hip. *J Bone Jt Surg Br*. 2005;87(June (6)):844–850.
- Saleh Khaled J, Kassim R, Yoon P, Vorlicky LN. Complications of total hip arthroplasty. *Am J Orthop (Belle Mead, NJ)*. 2002;31(8):485–488.
- Song KH, Kim ES, Kim Yk Jin HY, et al. Differences in the risk factors for surgical site infection between total hip arthroplasty and total knee arthroplasty in the Korean Nosocomial Infections Surveillance System (KONIS). *Infect Control Hosp Epidemiol*. 2012;33(November (11)):1086–1093.
- Talmo Carl T, Robbins Claire E, Bono James V. Total joint replacement in the elderly patient. *Clin Geriatr Med*. 2010;26(3):517–529.
- Triantafyllopoulos G, Studner O, Memtsoudis S, Poultsides LA. Patient, surgery, and hospital related risk factors for surgical site infections following total hip arthroplasty. *Sci World J*. 2015;2015:979560.
- Willis-Owen CA, Konyves A, Martin DK. Factors affecting the incidence of infection in hip and knee replacement: an analysis of 5277 cases. *J Bone Jt Surg Br*. 2010;92(August (8)):1128–1133.