



Original research

Surgical site infection and transfusion rates are higher in underweight total knee arthroplasty patients

Jorge Manrique, MD, Antonia F. Chen, MD, MBA^{*}, Miguel M. Gomez, MD, Mitchell G. Maltenfort, PhD, William J. Hozack, MD

Rothman Institute at Thomas Jefferson University, Philadelphia, PA, USA

ARTICLE INFO

Article history:

Received 7 February 2016

Received in revised form
30 March 2016

Accepted 31 March 2016

Available online 19 May 2016

Keywords:

Arthroplasty, replacement, knee

Body mass index

Perioperative complication

Prosthesis-related infections

Underweight

ABSTRACT

Background: Underweight (UW) patients undergoing total hip arthroplasty have exhibited higher complication rates, including infection and transfusion. No study to our knowledge has evaluated UW total knee arthroplasty (TKA) patients. We, therefore, conducted a study to investigate if these patients are at increased risk for complications, including infection and transfusion.

Methods: A case-control study was conducted using a prospectively collected institutional database. Twenty-seven TKA patients were identified as UW (body mass index [BMI] < 18.5 kg/m²) from 2000–2012 and were matched for age, gender, date of surgery, age-adjusted Charlson comorbidity index, rheumatoid arthritis, and diabetes. These patients were compared to 81 normal weight patients (BMI 18.5–24 kg/m²). Demographic variables were compared, along with wound complications, surgical site infection (SSI), blistering, deep vein thrombosis, pulmonary embolism, transfusion, revision, flexion contracture, hematoma formation, and patellar clunk.

Results: The average BMI was 17.1 kg/m² (range 12.8–18.4) for UW and 23.0 kg/m² (range 19.0–25.0) for normal weight patients ($P < .001$). UW TKA patients were more likely to develop SSIs (3/27, 11.1% vs 0/81, 0.0%, $P = .01$) and were more likely to require transfusions (odds ratio = 3.4, confidence interval 1.3–9.1; $P = .02$).

Conclusions: Our study demonstrates that UW TKA patients have a higher likelihood of developing SSI and requiring blood transfusions. The specific reasons are unclear, but we conjecture that it may be related to decreased wound healing capabilities and low preoperative hemoglobin. Investigation of local tissue coverage and hematologic status may be beneficial in this patient population to prevent SSI. Based on the results of this study, a prospective evaluation of these factors should be undertaken.

© 2016 Published by Elsevier Inc. on behalf of American Association of Hip and Knee Surgeons. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Body mass index (BMI) abnormalities have been closely associated with poorer outcomes in surgical patients. Most studies have focused on obese patients, as they comprise 34.9% of the adult population in the United States [1]. These patients have increased

readmission rates, a higher incidence of infections, and greater complication rates compared to normal weight (NW) patients [2–7]. However, much less is known regarding the outcomes of underweight (UW) surgical patients, since they only make up 2.3% of the US population and 0%–3.66% of patients in European nations [8,9].

In the field of general surgery, UW patients (BMI < 18.5 kg/m²) have a higher risk of mortality, morbidity, and poorer outcomes compared to overweight and obese patients [10–13]. With regard to total joint arthroplasty, UW total hip arthroplasty (THA) patients have been identified as having a higher incidence of infection, transfusion, dislocation, readmission, and mortality [2–4,14,15]. These patients also have been reported to have lower postoperative functional health scores [16].

Although specific studies have been conducted evaluating UW THA patients, no previous study has been performed evaluating

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to <http://dx.doi.org/10.1016/j.artd.2016.03.005>.

^{*} Corresponding author. 125 South 9th Street, Suite 1000, Philadelphia, PA 19107, USA. Tel.: +1 267 339 3605.

E-mail address: antonia.chen@rothmaninstitute.com

<http://dx.doi.org/10.1016/j.artd.2016.03.005>

2352-3441/© 2016 Published by Elsevier Inc. on behalf of American Association of Hip and Knee Surgeons. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

UW patients undergoing elective, primary, and total knee arthroplasty (TKA). Therefore, the purpose of this study was to investigate whether UW patients undergoing TKA are at increased risk for complications and poorer outcomes. We hypothesize that UW TKA patients have a higher rate of complications compared to NW TKA patients.

Material and methods

After institutional review board approval #08R.207, a retrospective, single institution, case-control study was conducted including patients from January 2000 to December 2012. We identified patients from our prospective institutional database that underwent primary TKA (International Classification of Diseases Ninth Revision procedure code: 81.54 and Current Procedural Terminology code: 27447). All patients had available weight and height data at the time of hospital admission. Patients were classified into the following groups: UW (BMI < 18.5 kg/m²), NW (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), or obese (30.0 kg/m²) [13]. We identified 27 UW patients that underwent primary, unilateral TKA, and each patient's electronic medical record was reviewed for verification of weight and height data obtained in the electronic query.

These UW patients were matched to a cohort of NW patients with similar demographic characteristics in a 3:1 ratio (81:27 patients). Matching was based on age (± 7 years), gender (male/female), date of surgery (± 5 years), Charlson comorbidity index age adjusted ([CCI] age adjusted, ± 3), the presence of diabetes (yes/no), and the presence of rheumatoid arthritis (RA, yes/no). CCI was used as it provides a quantification of health and predicts mortality [17]. Demographic and surgical variables, such as gender, CCI, length of hospital stay (LOS), preoperative and postoperative laboratory values, transfusions, and complications were recorded. Specific complications that were recorded in the chart included wound drainage, poor wound healing, surgical site infection (SSI), blistering, deep vein thrombosis, pulmonary embolism, dislocation, fracture, revision, flexion contracture development, and hematoma. These diagnoses were determined by the physician and treated accordingly. These complications are among those evaluated and included by the Complications Workgroup of the Knee Society [18]. The definition used for deep incisional SSI was the one specified by the Centers for Disease Control criteria [19]. The SSI criteria was used instead of the Musculoskeletal Infection Society and International Consensus Meeting definitions for periprosthetic joint infection [20] because the Musculoskeletal Infection Society and International Consensus Meeting criteria were not available during the entire duration of our study.

This states that the patient must have the infection occurring within 1 year if implant is in place, and the infection appears to be related to the operative procedure with involvement of deep soft tissues. In addition, it must include one of the following 3:

1. Purulent drainage from the deep incision of the surgical site.
2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever ($>38^{\circ}\text{C}$), localized pain, or tenderness, unless culture of the incision is negative.
3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of a deep incisional SSI by a surgeon or attending physician.

The study population had a mean age of 69.9 years (range 41.6–89.8) and was composed of 6 males and 21 females. The average BMI for this group was 17.0 kg/m² (range 12.8–18.4). The

control group had a mean age of 69.5 years (range 38.0–90.5), with 63 females and 18 males. The average BMI for the controls was 23.0 kg/m² (range 19.0–25.0). The follow-up average was 3.8 years (range 1.1–7.9 years) for UW patients and 5.3 for NW patients (range 1.0–13.6 years). There were no differences between the groups with regard to age (69.9 vs 69.5; $P = .90$), gender (80% female vs 80% female; $P = 1.0$), diabetes (6.7% vs 6.7%; $P = 1.0$), RA (29.6% vs 29.6%; $P = 1.0$), or CCI (4.2 vs 4.1; $P = .59$). Patients in the UW group had a lower BMI (17.0 kg/m² vs 22.9 kg/m²; $P < .001$), lower weight (51.6 kg vs 63.4 kg; $P < .001$), greater height (174 cm vs 165.0 cm; $P = .003$). Patients in both groups had a higher incidence of RA (29.6%) compared to the general population (1%) [21]. The demographic characteristics of all patients are shown in Table 1.

All patients were operated by any of 7 orthopaedic, arthroplasty fellowship-trained surgeons who all used the same protocol in the same hospital setting. The same preoperative and postoperative protocol guided management as per year of surgery. All surgeries were performed using a tourniquet, the approach was made through a medial parapatellar approach, and all knees were posterior-stabilized, cemented knees. No blood preserving elements, such as fibrin glue, sealants, or retransfusion drains, were used during the study period. Prophylactic antibiotic was administered to all patients within one hour preoperatively and for 24 hours postoperatively, as per protocol. Cefazolin was used routinely, but if a penicillin allergy was documented, vancomycin was used instead. Blood loss was calculated from the preoperative hematocrit (Hct) levels and Hct levels one day after the surgery, according to a previously validated formula presented by Rosencher et al. [22].

Statistical analysis

Statistical analysis was performed on continuous variables using Wilcoxon rank sum test and categorical variables were analyzed using Fischer's exact test. Logistic regression was used to determine the odds ratio (OR) for requiring postoperative transfusion in the UW patients. R 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria) was used for data analysis.

Results

UW TKA patients had a higher rate of SSI (3/27, 11.1%) compared with NW patients (0/81, 0%; 95% confidence interval [CI]: 0.0–4.0; $P = .01$). UW patients had an increased risk of SSI (OR: 23.3; 95% CI: 1.2–466.5; $P = .04$) compared with NW patients. The 3 patients who developed SSI in the UW group all underwent explantation and debridement, for an intended 2-stage exchange arthroplasty.

Preoperatively, UW patients had lower hemoglobin (Hb) (12.3 g/dL \pm 1.5) and Hct (36.8% \pm 4.3) levels than NW patients (Hb 13.0 g/dL \pm 1.3, $P = .04$; Hct 39.0% \pm 3.4, $P = .01$). Postoperative Hb (8.8 g/dL \pm 1.0), and Hct (26.6% \pm 3.0) was also lower in UW

Table 1
Patient demographics.

Demographics	Underweight, n = 27	Normal weight, n = 81	P-value
Age, mean (y)	69.9 \pm 13.6	69.5 \pm 13.4	.90
Gender			
Male	6	18	1
Female	21	72	
Weight, mean (kg)	51.6 \pm 7.9	63.4 \pm 9.2	<.001
Height, mean (cm)	174.0 \pm 15.7	165.6 \pm 9.5	.01
BMI, mean (kg/m ²)	17.0 \pm 7.9	23.0 \pm 1.5	<.001
CCI age adjusted, mean	4.2 \pm 1.3	4.1 \pm 1.4	.59
Rheumatoid arthritis	8	24	1
Diabetes	2	6	1

patients compared with NW patients (Hb: 9.6 g/dL ± 1.2, P = .003; Hct: 28.7% ± 3.6, P = .01). Although the calculated blood loss in UW patients (403.9 mL ± 168.0) was similar to NW patients (435.4 mL ± 165.5, P = .39), UW patients were more likely to require postoperative allogenic transfusion (10/27, 37.0%) compared with NW patients (12/81, 13.2%; OR = 3.4, 95% CI 1.3-9.1; P = .02).

No difference was observed between the 2 groups regarding LOS, deep vein thrombosis, pulmonary embolism, dislocation, fracture, aseptic revision, development of flexion contracture, hematoma, or patellar clunk (Table 2).

Discussion

This is the first study that evaluates complications in UW TKA patients, and it suggests that they have an increased risk of developing SSI and may have low preoperative Hb and Hct requiring an allogenic blood transfusion despite a similar blood loss. These findings are similar to studies in the general surgery literature that have found that UW patients have greater complications than other patients. UW patients undergoing coronary artery bypass graft surgery have been found to have longer intensive care unit stays and longer LOS compared with NW patients [12]. UW minority patients evaluated through the American College of Surgeons' National Surgical Quality Improvement Program Participant Use Data File exhibited higher mortality and postoperative complications than overweight and NW patients. A higher incidence of wound problems and deep SSI was also observed postoperatively [11]. There is an established association between low BMI and poor surgical outcomes in a variety of disciplines [10-12,23-30]. Higher transfusion rates were observed among UW patients after surgical intervention following hip fracture repair and general surgery patients [10,11]. Furthermore, mortality was observed to increase, up to 3 fold, in UW patients after lower extremity bypass surgery compared with NW patients [31].

In our patient population, UW patients were more likely to undergo allogenic blood transfusions, most likely secondary to a low preoperative Hb level rather than due to increased surgical blood loss. Postoperative allogenic transfusion has been

demonstrated to be a risk factor for developing infections [32]. The increased rate of allogenic blood transfusions in our UW patients may play a role in the increased incidence of SSI. Interestingly, 2 of the 3 patients that were infected received a blood transfusion. However, because of the low numbers, this could not be separately analyzed. Our results concur with those of Alfonso et al. [4], who found that UW patients who underwent THA required more blood transfusions. Furthermore, Zhang et al. [3] observed that these types of patients had a greater number of revisions and complications, similar to the rates found in high BMI patients. Although both UW and NW patients demonstrated similar amounts of blood loss after TKA, the preoperative Hb and Hct levels were significantly lower for UW patients, thus placing them at higher risk of needing a transfusion postoperatively. Preoperative optimization of Hb and Hct is a potentially modifiable risk factor for reducing transfusion rates by using agents such as erythropoietin before TKA, which may be beneficial as per recommendation of the Network of Advancement of Transfusion Alternatives [33]. These recommendations suggest that the use of erythropoiesis-stimulating agents can be beneficial in patients undergoing elective orthopaedic procedures. A previously performed systematic review showed that patients undergoing cardiac and orthopaedic surgery demonstrated a reduction in allogenic transfusions (OR = 0.42) when erythropoietin was used [34]. Further investigation is warranted to evaluate using these agents in UW TKA patients before surgery.

Another potential risk factor for developing infection in UW TKA patients is that these patients have reduced subcutaneous fat that could predispose the overlying skin to be less resistant and more vulnerable to dehiscence or necrosis. This may be especially true in TKA patients who have very little subcutaneous tissue over diarthrodial joints, as the correlation between BMI and subcutaneous adipose skin thickness has been seen in other studies [35]. One of the 3 infected patients required a gastrocnemius flap due to wound problems, possibly reflecting deficient overlying soft tissue. One other possibility for increased infection risk is poor nutritional status with subsequent decreased capability for wound healing [36]. A lower BMI may be an indirect measure of nutritional status, as lower BMI patients have been shown to have lower levels of albumin, prealbumin, and/or protein [37]. Low BMI patients have decreased reserves and an inability to accurately react to stress because they have suppressed immune systems [38]. Low BMI has also been associated with higher morbidity and mortality rates, possibly reflecting an altered physiological state [39]. Only 8 UW patients had nutritional data, and there was no evidence of a nutritional problem in these patients and no subcutaneous tissue measurements were performed. As such, our study could not establish an association of these factors to SSI. Not all patients had presurgical albumin or other nutritional markers. Although this would have been optimal, at the time of the study period, not all patients were worked up for nutritional deficiencies. This aspect is controversial because if patients exhibit altered nutritional status, surgical intervention could differ and these patients may not have been included in our study.

This study has several limitations. Its retrospective nature limits the data obtained in our study to what is available in patient charts. Although we acknowledge the importance of additional information, such as nasal *Staphylococcus* screening and preoperative medications, these were not included because of lack of consistency in recorded data. Furthermore, there is a low number of UW patients despite the extensive database search performed that included different Current Procedural Terminology codes to avoid missing patients that meet inclusion criteria. A larger multicenter study might be needed to increase this number. One of the reasons for low numbers is the low incidence of UW patients in our population. It could also reflect the decision of not performing elective

Table 2
Results.

Results	Underweight, n = 27	Normal weight, n = 81	P-value
Length of stay, mean ± SD (d)	3.7 ± 1	3.4 ± 1.2	.2
Preoperative hemoglobin, mean ± SD (mg/dL)	12.3 ± 1.5	13.0 ± 1.3	.04 ^a
Preoperative hematocrit, mean ± SD (%)	36.8 ± 4.3	39.0 ± 3.4	.03 ^a
Postoperative hemoglobin, mean ± SD (mg/dL)	8.8 ± 1.0	9.6 ± 1.2	.002 ^a
Postoperative hematocrit, mean ± SD (%)	26.6 ± 3	28.7 ± 3.6	.006 ^a
Estimated blood loss	403.9 ± 168.0	435.4 ± 165.5	.40
Allogenic blood transfusion, n	10	12	.01 ^a
Wound drainage, n	3	3	.16
SSI, n	3	0	.01 ^a
Blistering, n	0	0	1.0
Pulmonary embolism, n	0	1	1.0
Aseptic revision, n	1	3	1.0
Flexion contracture, n	1	1	.44
Deep vein thrombosis, n	0	1	1.0
Dislocation, n	0	0	1.0
Fracture, n	0	0	1.0
Hematoma, n	0	0	1.0
Patellar clunk, n	0	0	1.0

SD, standard deviation.

^a Statistically significant.

surgery on UW patients that were not considered optimal surgical candidates. Moreover, nutritional data, such as laboratory studies and nutritional consults, were not routinely ordered in the past; therefore, these values could not be included in our study. In addition, patients were only matched by RA, diabetes mellitus, and CCI, as these conditions are considered to be a surrogate marker for surgical risk based on comorbidities to assess for individual risk factors. Because multiple surgeons were involved in this study, there may have been various surgical techniques that can affect blood loss. In addition, there were no uniform transfusion triggers, and each individual surgeon transfused based on a combination of laboratory tests and clinical symptoms. Finally, follow-up was limited to clinical appointments documented in the electronic medical record, and patients were not contacted by phone.

Conclusions

Despite these limitations, our study demonstrated that UW TKA patients had a higher rate of SSI compared with NW patients. Although the exact reason for this finding is not known, it may be related to wound healing capabilities and the need for transfusions, as these patients had low preoperative Hb and Hct levels. UW patients undergoing TKA may benefit from preoperative optimization to reduce the risk of sustaining SSIs.

References

- [1] Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA* 2014;311:806.
- [2] Saucedo JM, Marecek GS, Wanke TR, et al. Understanding readmission after primary total hip and knee arthroplasty: who's at risk? *J Arthroplasty* 2014;29:256.
- [3] Zhang Z, Zhao X, Kang Y, et al. The influence of body mass index on life quality and clinical improvement after total hip arthroplasty. *J Orthop Sci* 2012;17:219.
- [4] Alfonso DT, Howell RD, Caceres G, Kozlowski P, Di Cesare PE. Total hip arthroplasty in the underweight. *J Arthroplasty* 2008;23:956.
- [5] Workgroup of the American Association of Hip and Knee Surgeons Evidence Based Committee. Obesity and total joint arthroplasty: a literature based review. *J Arthroplasty* 2013;28:714.
- [6] Wolfe F, Michaud K. Effect of body mass index on mortality and clinical status in rheumatoid arthritis. *Arthritis Care Res (Hoboken)* 2012;64:1471.
- [7] Lash H, Hooper G, Hooper N, Frampton C. Should a patients BMI status be used to restrict access to total hip and knee arthroplasty? functional outcomes of arthroplasty relative to BMI - single centre retrospective review. *Open Orthop J* 2013;7:594.
- [8] Costa-Font J, Jofre-Bonet M. Anorexia, body image and peer effects: evidence from a sample of European women. *Economica* 2013;80:44.
- [9] Fryar CD, Ogden CL. Prevalence of underweight among adults aged 20 and over: United States, 1960–1962 through 2011–2012. Atlanta, GA: National Center for Health Statistics; September 2014.
- [10] Batsis JA, Huddleston JM, Melton LJ, et al. Body mass index and risk of adverse cardiac events in elderly patients with hip fracture: a population-based study. *J Am Geriatr Soc* 2009;57:419.
- [11] Nafiu OO, Ramachandran SK, Wagner DS, Campbell DA, Stanley JC. Contribution of body mass index to postoperative outcome in minority patients. *J Hosp Med* 2012;7:117.
- [12] Atalan N, Fazliogulları O, Kunt AT, et al. Effect of body mass index on early morbidity and mortality after isolated coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth* 2012;26:813.
- [13] Flegal KM, Kit BK, Graubard BI. Body mass index categories in observational studies of weight and risk of death. *Am J Epidemiol* 2014;180:288.
- [14] Somayaji R, Barnabe C, Martin L. Risk factors for infection following total joint arthroplasty in rheumatoid arthritis. *Open Rheumatol J* 2013;7:119.
- [15] Ringbäck Weitoft G, Eliasson M, Rosén M. Underweight, overweight and obesity as risk factors for mortality and hospitalization. *Scand J Public Health* 2008;36:169.
- [16] Sanmartin C, McGrail K, Dunbar M, Bohm E. Using population data to measure outcomes of care: the case of hip and knee replacements. *Health Rep* 2010;21:23.
- [17] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373.
- [18] Iorio R, Della Valle CJ, Healy WL, et al. Stratification of standardized TKA complications and adverse events: a brief communication. *Clin Orthop Relat Res* 2014;472:194.
- [19] Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999;27:97. quiz 133–4; discussion 96.
- [20] Parvizi J, Gehrke T. Definition of periprosthetic joint infection. *J Arthroplasty* 2014;29:1331.
- [21] Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Arthritis Rheum* 2008;58:15.
- [22] Rosencher N, Kerckamp HEM, Macheras G, et al. Orthopedic surgery transfusion hemoglobin european overview (OSTHEO) study: Blood management in elective knee and hip arthroplasty in Europe. *Transfusion* 2003;43:459.
- [23] Allen JG, Arnaoutakis GJ, Weiss ES, et al. The impact of recipient body mass index on survival after lung transplantation. *J Heart Lung Transplant* 2010;29:1026.
- [24] Ndrepepa G, Keta D, Byrne RA, et al. Impact of body mass index on clinical outcome in patients with acute coronary syndromes treated with percutaneous coronary intervention. *Heart Vessels* 2010;25:27.
- [25] Giles KA, Hamdan AD, Pomposelli FB, et al. Body mass index: surgical site infections and mortality after lower extremity bypass from the National Surgical Quality Improvement Program 2005–2007. *Ann Vasc Surg* 2010;24:48.
- [26] Lederer DJ, Wilt JS, D'Ovidio F, et al. Obesity and underweight are associated with an increased risk of death after lung transplantation. *Am J Respir Crit Care Med* 2009;180:887.
- [27] Smith BG, Hakim-Zargar M, Thomson JD. Low body mass index: a risk factor for superior mesenteric artery syndrome in adolescents undergoing spinal fusion for scoliosis. *J Spinal Disord Tech* 2009;22:144.
- [28] Suemitsu R, Sakoguchi T, Morikawa K, et al. Effect of Body Mass Index on Perioperative Complications in Thoracic Surgery. *Asian Cardiovasc Thorac Ann* 2008;16:463.
- [29] van Venrooij LMW, de Vos R, Borgmeijer-Hoelen MMMJ, Haaring C, de Mol BAJM. Preoperative unintended weight loss and low body mass index in relation to complications and length of stay after cardiac surgery. *Am J Clin Nutr* 2008;87:1656.
- [30] Sharma S, Fraser M, Lovell F, Reece A, McLellan AR. Characteristics of males over 50 years who present with a fracture: epidemiology and underlying risk factors. *J Bone Joint Surg Br* 2008;90:72.
- [31] Scuderi GR. The stiff total knee arthroplasty. *J Arthroplasty* 2005;20:23.
- [32] Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic joint infection: the incidence, timing, and predisposing factors. *Clin Orthop Relat Res* 2008;466:1710.
- [33] Goodnough LT, Maniatis A, Earnshaw P, et al. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. *Br J Anaesth* 2011;106:13.
- [34] Laupacis A, Fergusson D. Erythropoietin to minimize perioperative blood transfusion: a systematic review of randomized trials. The International Study of Peri-operative Transfusion (ISPOT) Investigators. *Transfus Med* 1998;8:309.
- [35] Akkus O. Evaluation of skin and subcutaneous adipose tissue thickness for optimal insulin injection. *J Diabetes Metab* 2012;3:8.
- [36] Zorrilla P, Gómez LA, Salido JA, Silva A, López-Alonso A. Low serum zinc level as a predictive factor of delayed wound healing in total hip replacement. *Wound Repair Regen* 2006;14:119.
- [37] Horwich TB, Kalantar-Zadeh K, MacLellan RW, Fonarow GC. Albumin levels predict survival in patients with systolic heart failure. *Am Heart J* 2008;155:883.
- [38] Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. *Am J Surg* 1980;139:160.
- [39] Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. *JAMA* 2005;293(15):1861.