Perioperative Patient-specific Factors-based Nomograms Predict Short-term Periprosthetic Bone Loss After Total Hip Arthroplasty

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Abstract

Background

Although medical intervention of periprosthetic bone loss in the immediate postoperative period was recommended, not all the patients experienced periprosthetic bone loss after total hip arthroplasty (THA). Prediction toolsthat enrolledallpotential risk factors to calculate an individualized prediction of postoperative periprosthetic bone loss were strongly needed for clinical decision-making.

Methods

Data of the patients underwent primary unilateral cementless THA between April 2015 and October 2017 in our center were retrospectively collected. Candidate variables included demographic data and bone mineral density (BMD) in spine, hip and periprosthetic regions that measured 1 week after THA. Outcomes of interest included the risk of postoperative periprosthetic bone loss in Gruen zone 1, 7 and total zones in the 1st postoperative year. Nomograms were presented based on multiple logistic regressions via R language.Bootstrap was used for internal validation.

Results

427 patients (195 male and 232 female) were included in this study.The mean BMD of Gruen zone 1, 7,and total were decreased by 4.1%, 6.4%, and 1.7% at the 1st year after THA, respectively. 61.1% of the patients (261/427) experienced bone loss in Gruen zone 1 at the 1st postoperative year, while there were 58.1% (248/427) in Gruen zone 7 and 63.0% (269/427) in Gruen zone total. Bias-corrected c-index for risk of postoperative bone lossin Gruen zone 1, 7 and total zones in the 1st postoperative year were 0.700, 0.785, and 0.696, respectively. The most highly influential factor for the postoperative periprosthetic bone loss was the BMD in the corresponding Gruen zones at the baseline.

Conclusions

The present study presented the perioperative factors-based nomograms for predicting periprosthetic bone loss after THA with adequate predictive discrimination and calibration.Those tools would helpsurgeons to identify high-risk patients who may benefit from anti-bone-resorptive treatment on the early postoperative period effectively. Such prediction model could also provide patients with reasonable expectations following surgery, which may improve satisfaction and patient compliance.

Introduction

Total hip arthroplasty (THA) is the most effective therapy for end-stage hip diseases. Over 500,000 THAs were performed in the USA annually, and the demand for THA is still growing[1].As one of the major concerns after THA, periprosthetic bone loss was closely related to aseptic loosening, periprosthetic fractures, and implant failure[2].It was reported that the mean periprosthetic bone loss was up to 21.9% 10 years post-operation[3, 4]. Thus, medical intervention of periprosthetic bone loss in the immediate postoperative period was widely accepted[5, 6]. However, not all the patients experienced periprosthetic bone loss after THA, especially those without osteopenia and osteoporosis[7, 8].Correspondingly, identification of patients with increasedrisk of postoperative periprosthetic bone loss is of great value for clinical decision-makingand cost-effectiveness analysis on a patient-specific level.

Many patient-specific and surgery-related factors were closely related withincreased risk of postoperative prosthetic bone loss, including age[9], body mass index (BMI)[10], primary diagnosis[11], femoral stem design[12], preoperative bone mineral density (BMD) in hip and spine[13], periprosthetic BMD measured in the immediate postoperative period[14], and the administration of anti-osteoporosis agents[5]. Knowledge of these variables, however, only provides the surgeons with an individual factor that improves or worsensspecific outcome. No study yet has provided a comprehensive tool that enablesa quantified individualized risk prediction of postoperative periprosthetic bone losson bias ofnumerous variables. Thus, the purpose of the present study was to create perioperative patient-specific factors-basednomograms for postoperative periprosthetic bone loss prediction,which were applicable before the medical intervention.

Patients And Methods

The electronic medical records were retrospectively reviewed to identify patients who underwent primary unilateral cementless THA between April 2015 and October 2017 in the Center of Orthopedics, Guangdong Provincial Peoples' Hospital. The exclusion criteria included 1) inflammatory arthritis; 2) previous history of trauma or surgery in the involved hip; 3) periprosthetic fracture or infection; 4) secondary osteoporosis or other bone metabolism disorders; 5) absence of *intact* data of periprosthetic BMD measurement. We used the TRIPOD checklist when writing our report[15].

Data collection

Data of all the patients were retrospectively retrieved from the database of Guangdong Provincial People's Hospital. Patient demographics, preoperative BMD of hip and spine, BMD of 7 Gruen zones measured one-week after THA, surgical details and preoperative bone metabolic markers were collected. Outcomes included the BMD of Gruen zone 1, 7,and total zones measured one year after THA.

BMD measurement

BMD of proximal femur and lumbar spine (from L1 to L4) was measured using Dual-energy X-ray Absorptiometry (DEXA, LUNAR DPXMD#5966, Madison, WI, USA). The periprosthetic BMD of the femoral component was analyzed according to the protocol proposed by Gruen et al[16]. Briefly, the proximolateral,lateromedial, and distolateral regionsweredefined as Gruen zone 1, 2, and 3, respectively. Correspondingly, the medial periprosthetic region was divided into Gruen zone 5, 6, and 7 from the proximal to distal femur. Gruen zone 4 was located at least 1 cm distal to the tip of the stem (Fig 1). The total periprosthetic BMD was defined as the mean of BMD from zones 1 to 7. In the present study, the mean least significant changes (LSC) of the hip, spine, and periprosthetic Gruen zones were 0.017 ± 0.013 g/cm^2, 0.007 ± 0.005 g/cm^2, and 0.012 ± 0.015 g/cm^2, respectively.

Sample size

There is no golden standard approach to estimate the sample size requirements for risk prediction models till now. It was widely accepted at least 10 events per candidate variable for the derivation of a risk prediction model[17]. As 13 candidate variables were included for the regression analysis, at least 130 patients with observed positive outcomes (bone loss in Gruen zone 1, 7, or total in the 1st postoperative year) were required for the present study.

Statistical analysis

Continuous data was expressed as mean ± standard deviation or median with interquartile range. Categorical data was present as count (percent). Prediction models for the binary outcomes were created using multivariable logistic regression. As described in the previous study, candidate variables included in the nomograms were identified in a screening step with the P values < 0.3 that obtained bymultivariable analysis[18].

R version 3.5.0 (R Foundation for Statistical Computing) withspecific package (rms)was utilized for all statistical testing. For the binary outcomes, each final model achieved the maximum bias-corrected concordance index (c-index). 1000 bootstrap samples were drawn to correct the bias, and the final model fit each sample. Predicted probabilities were obtained for the original sample based on each bootstrap estimated model and a c-index calculated. The bias-corrected c-indexwas defined as the average of these bootstrap c indices. Additionally, model calibration was assessed by plotting the proportion of patients predicted to develop each outcome vs the actual proportion who developed each outcome for the original sample (apparent) and the bootstrap samples (bias-corrected).

Results

Descriptive Data

563 patients underwent primary unilateral cementless THA between April 2015 and October 2017 in our center. After the exclusion, a total of 427 patients (195 male and 232 female) were included in this study (Fig 2). Mean age of the patients was 59.3, with 94.1% married and 39.6% current or former smokers. Average BMI was 23.4. The most common comorbidity was hypertension (36.3%). The most common diagnosis was femoral head necrosis (49.6%), followed by femoral neck fractureand hip osteoarthritisin 22.7% and 17.8%, respectively. 20.4% of the patients underwent anti-osteoporosis treatment one year before the surgery, including zoledronate, alendronate, and teriparatideadministration. Pre-operative BMD in hip and spine were 0.881g/cm^2 and 0.828g/cm^2, respectively.

Preoperative Harris score of the involved hip was 41.7. The mean value of serum ALP was 74.9U/L, while the serum Ca was 2.31 mmol/L. Details of the demographic data were shown in Table 1.

All the surgeries were performed by the corresponding authors of the present study (QJZ and YCM). A standard posterolateral surgical approach was used. The femoral prosthesis used in the present study included the straight stem (Ribbed® classic; Waldemar Link GmbH, Germany) and the anatomic stem (L.C.U. ® classic; Waldemar Link GmbH, Germany). The CombiCup® was used for acetabular component (Waldemar Link GmbH, Germany). Partial weight bearing was required 1 week after THA, and full weight bearing was allowed 2 weeks after THA.

The mean BMD of Gruen zone 1, 7,and total were decreased by 4.1%, 6.4%, and 1.7% at the 1st year after THA, respectively (Table 2). 61.1% of the patients (261/427) experienced bone loss in Gruen zone 1 at the 1st postoperative year, while there were 58.1% (248/427) in Gruen zone 7 and 63.0% (269/427) in Gruen zone total. Figures 3 to 5 showed the nomogram prediction tools for the various outcomes.

Predictors for the risk of postoperative periprosthetic bone loss

Bone loss in Gruen zone 1 (Figure 3; Table3) was predicted by age, gender, diagnosis, history of anti-osteoporosis treatment, preoperative MNA-SF score, serum ALP and Ca concentration, and 1-weekpost-operative BMD of Gruen zone 1. The result of the validation showed good calibration. The model accurately discriminated the risk of the patients 70.0% of the time (bias-corrected C-index = 0.700). For bone loss in Gruen zone 7 (Figure 4; Table3), the significant predictors included gender, diagnosis, preoperative hip BMD, Harris score, and BMD of Gruen zone 7 measured one week after THA. The model accurately discriminatedthe risk of the patients 78.5% of the time (bias-corrected C-index = 0.785). In regard to bone loss in Gruen zone total(Figure 5; Table3), the significant predictors included diagnosis,implant design, BMI, preoperative hip BMD, serum ALP concentration, and 1-week post-operativeBMD of Gruen zone Total. The bias-corrected C-index of this model was 0.696.

Discussion

As majority of the femoral stems for primary THA were designed as proximally coated[19], the changes of proximal periprosthetic BMD,namely Gruen zone 1 and 7 (Fig 1), were suggested to bemore clinically relevant than those of other Gruen zones. In consistent with our results, previous studyalso found that the decreasesof the mean BMD in Gruen zone 1 and 7 variedfrom 5% to 10% during the first two years after THA[7].As the mean changes of BMD inGruen zone 1 (−0.033 g/cm^2), Gruen zone 7 (−0.057 g/cm^2),and total Gruen zones (−0.025 g/cm^2)were larger than the LSC (0.012 g/cm^2), we believe that our results represent a real biological change[20].

As we mentioned before, not all the patients experienced periprosthetic bone loss after THA[7, 8], while earlymedical intervention was recommended[5, 6].However, no predictive tool that enablesquantified individualized risk evaluations of postoperative periprosthetic bone loss on bias of numerous variableswas available till now.Nomograms are a pictorial representation of a complex mathematical formula designed to allow the approximate graphical computation[21]. Points at respective horizontal axis in nomograms represented the predictive value of the variables. After calculation of the total risk score based on the patients' response for each variable, surgeons could correlate it to a specific chance of having the given outcome. Recently, nomograms have been used widely in predicting clinical related outcomes after total joint arthroplasty, such as 30-day/90-day readmission[22, 23], major complications[24], and excess cost within bundled payment[25]. Those prediction modelsthatindividualized the predicted outcome to specific patients' characteristics performed better than simply relying on the average outcome[18]. To the best of our knowledge, our study represented the first time to use the nomograms in estimating the risk of periprosthetic bone loss. In the present study, variables (age, BMI, implant design, et al.) that have been reported to be potential risk factors of postoperative periprosthetic BMD decreaseswere retrospectively collected to create the nomograms[9-14]. The concordance index in binary outcomes predicting models represents the ability to distinguish between patients who experience an event from those who do not. It is measured on a scale of 0.5 (no better than chance) to 1 (perfect discrimination)[21]. As the bias-corrected concordance index of Gruen zone 1, 7 and total ranged from 0.696-0.785 in the present study, we proposed that those nomograms estimating the risk of periprosthetic bone loss had moderate to strong discrimination[21].

In the present study, we found that the most highly influential factor for postoperative bone loss in Gruen zone 1, 7 and total zones was BMD in corresponding Gruen zones measured one week after THA. As we discussed in our previous study[14], the trabecular bone of proximal femur became granular shaped and was located mostly in the interface between the implant and host bone after implantation of the femoral prosthesis. Similar to autogenous cancellous bone grafting, the trabecular bone would be completely eliminated before the new bone formation, which we supposed to be a reasonable explanation[26]. Previous study demonstrated that younger patients have more postoperative daily living activities and corresponding accelerated periprosthetic bone remolding[27]. Similarly, we also found that age was negatively related to the postoperative bone loss in Gruen zone 1, 7, and total zones. In consistent with previous studies[13, 28], preoperative hip BMD was found to be predictable of less postoperative periprosthetic bone loss in the present study. Similar to our results, the meta-analysis reported that patients using straight stems experienced less bone loss than those using anatomic designs at the 1-year time point[12]. Nevertheless, further studies with larger scale and specific stem design groupings are necessary to determine its' clinical relevance, as cementless anatomic stems were reported to be with satisfied survival rate at 10 years (>95%)[29].

Bisphosphonate is a class of anti-bone-resorptive agents including alendronate, risedronate, ibandronate, and zoledronic acid, et al. FDA-approved indications for bisphosphonates include treatment of osteoporosis in postmenopausal women, osteoporosis in men, glucocorticoid-induced osteoporosis, hypercalcemia of malignancy, Paget disease of the bone, and malignancies with metastasis to the bone[30]. Recently, several prospective studies demonstrated that the administration of bisphosphonate effectively inhibited postoperative periprosthetic bone loss from one to three years after the THA[13, 31-34]. However, there is no clear guideline regarding the indication of bisphosphonate treatment for patients underwent THA, especially for those without osteoporosis and osteopenia. Traditionally, clinicians used their individual or group evaluation of the risk of postoperative periprosthetic bone loss as the basis of making clinical decisions, which has been proven to be subject to biases[18]. A prediction model that allows estimation of postoperative periprosthetic BMD changes at perioperative period could enable efficient identification of patients who benefit more from bisphosphonate treatment and individualized decision-making. Such prediction model could also provide patients with reasonable expectations following surgery, which may improve satisfaction and patient compliance.

Our study also subjected to some limitations. Firstly, patientsenrolledin the present study were relatively young (63, (51, 67) years, presented as median (Q1, Q3)). External validation is needed before the application of those nomograms on older (>80 yrs.) or much younger patients (<40 years).Secondly, although the sample size of the present study has met the requirement of the statistics, we admitted that large-scale sample is needed for building nomograms with higher discrimination and calibration. Additionally, the present study included a relatively short follow-up period. Nevertheless, it was reported that the periprosthetic bone loss was most evident and clinically relevant in the first year after THA,as the initial periprosthetic bone remodeling process was mainly completed in the first 12 postoperative months[4, 35]. Lastly, although the data was collected from a high-volume joint center that has a complex patient population, selection bias still existed due to the retrospective, single-center design.

Conclusion

Our study presented the perioperative patients-specific factors-based nomograms for predicting periprosthetic bone loss after THA. As those nomograms showed adequate predictive discrimination and calibration, we believe that those tools would helpsurgeons to identify high-risk patients who may benefit from anti-bone-resorptive treatment on the early postoperative period effectively. Such prediction model could also provide patients with reasonable expectations following THA, which may improve satisfaction and patient compliance.

List Of Abbreviations

THA, Total hip arthroplasty

BMI, Body mass index

BMD, Bone mineral density

DEXA, Dual-energy X-ray Absorptiometry

LSC, Least significant changes

Declarations

Ethics approval and consent to participate

Institutional review board approval of Guangdong Provincial Peoples' Hospital was obtained. Signed informed consent for participation was obtained from all study patients.

Consent for publication

Signed informed consent for publication was obtained from all study patients.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Study design: Guangtao Fu and Qiujian Zheng. Surgery performance: Yuanchen Ma and Qiujian Zheng. Data collection: Mengyuan Li and Qingtian Li. Data analysis and data interpretation: Yunlian Xue. DEXA analysis: Zhantao Deng. Drafting manuscript: Guangtao Fu. Revising manuscript content: Mengyuan Li and Yuanchen Ma. Approving final version of manuscript: Qiujian Zheng. Qiujian Zheng takes responsibility for the integrity of the data analysis.

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Tables

Table 1
Demographic data

Variables	Prevalenceor average
Age (years)	59.3±10.8
Male	45.7% (195/427)
Married	94.1% (402/427)
BMI (kg/m^2)	23.4±3.8
Current/former smoker	39.6% (169/427)
Comorbidities	
Diabetes mellitus	17.3% (74/427)
Hypertension	36.3% (155/427)
Stroke	6.8% (29/427)
Heart dysfunction	8.7% (37/427)
Others *	17.1% (73/427)
Diagnosis	
Femoral neck fracture	22.7% (97/427)
Femoral head necrosis	49.6% (212/427)
Hip osteoarthritis	17.8% (76/427)
Developmental dysplasia of the hip	9.8% (42/427)
History of anti-osteoporosis therapy in the last year	20.4% (87/427)
Preoperative systematic BMD	
Spine (g/cm^2)	0.881±0.150
Hip (g/cm^2)	0.828±0.181
Serum ALP (U/L)	74.9±25.6
Serum calcium (mmol/L)	2.31±0.12
Preoperative Harris score of the involved hip	41.7±19.9
Femoral component design	
Straight stem	65.1% (278/427)
Anatomic stem	34.9% (149/427)

Table 2
Main outcomes

	n	1 week postoperative	n	1 year postoperative	n	Change (1 week – 1year postoperative)
BMD of Gruen zone 1 (g/cm^2)	427	0.801 (0.717, 0.891)	427	0.768 (0.702, 0.842)	427	-0.033 (-0.116, 0.044)
BMD of Gruen zone 7 (g/cm^2)	427	0.889 (0.716, 1.094)	427	0.807 (0.729, 0.97)	427	-0.057 (-0.157, 0.072)
BMD of Total Gruen zones (g/cm^2)	427	1.44 (1.323, 1.519)	427	1.395 (1.286, 1.482)	427	-0.025 (-0.09, 0.024)
Results were presented as median (Q1, Q3).						

Table 3
Results of the logistic regression

	ROI 1			ROI 7			ROI total		
	Coefficient	Standard Error	P Value	Coefficient	Standard Error	P Value	Coefficient	Standard Error	P Value
Age	-0.080	0.035	0.023	0.033	0.035	0.346	-0.020	0.027	0.454
Gender	-1.518	0.642	0.018	-0.856	0.763	0.262	-0.005	0.588	0.993
History of anti-osteoporosis treatment	-1.635	0.848	0.054	0.497	0.991	0.616	0.132	0.763	0.863
BMI	-0.027	0.067	0.687	0.012	0.077	0.877	-0.144	0.071	0.042
Diagnosis 1(transform into dummy variable)	1.687	1.016	0.097	0.934	1.006	0.353	0.805	0.847	0.342
Diagnosis 2(transform into dummy variable)	-1.198	0.989	0.226	-1.949	1.031	0.059	-1.420	0.892	0.111
Diagnosis 3(transform into dummy variable)	-1.220	0.659	0.064	-0.685	0.772	0.375	-1.532	0.658	0.02
MNA-SF score	0.499	0.364	0.170	-0.148	0.397	0.709	-0.097	0.320	0.762
Preoperative lumbar BMD	-2.910	2.819	0.302	2.483	3.061	0.417	0.719	2.512	0.775
Preoperative hip BMD	-1.197	2.604	0.646	-8.550	3.124	0.006	-3.161	2.275	0.165
Serum ALP	-0.017	0.013	0.180	-0.001	0.015	0.949	-0.018	0.012	0.154
Serum Ca	-4.608	2.922	0.115	-0.849	3.065	0.782	0.107	2.624	0.967
Preoperative Harris score	0.010	0.018	0.569	0.044	0.020	0.030	0.005	0.017	0.751
Implant design of femoral component	0.136	0.750	0.857	0.277	0.739	0.708	1.655	0.768	0.031
BMD of ROI 1 at 1 week after THA	7.012	2.715	0.010	/	/	/	/	/	/
BMD of ROI 7 at 1 week after THA	/	/	/	10.658	2.389	<0.001	/	/	/
BMD of ROI total at 1 week after THA	/	/	/	/	/	/	5.705	2.461	0.020

Figures

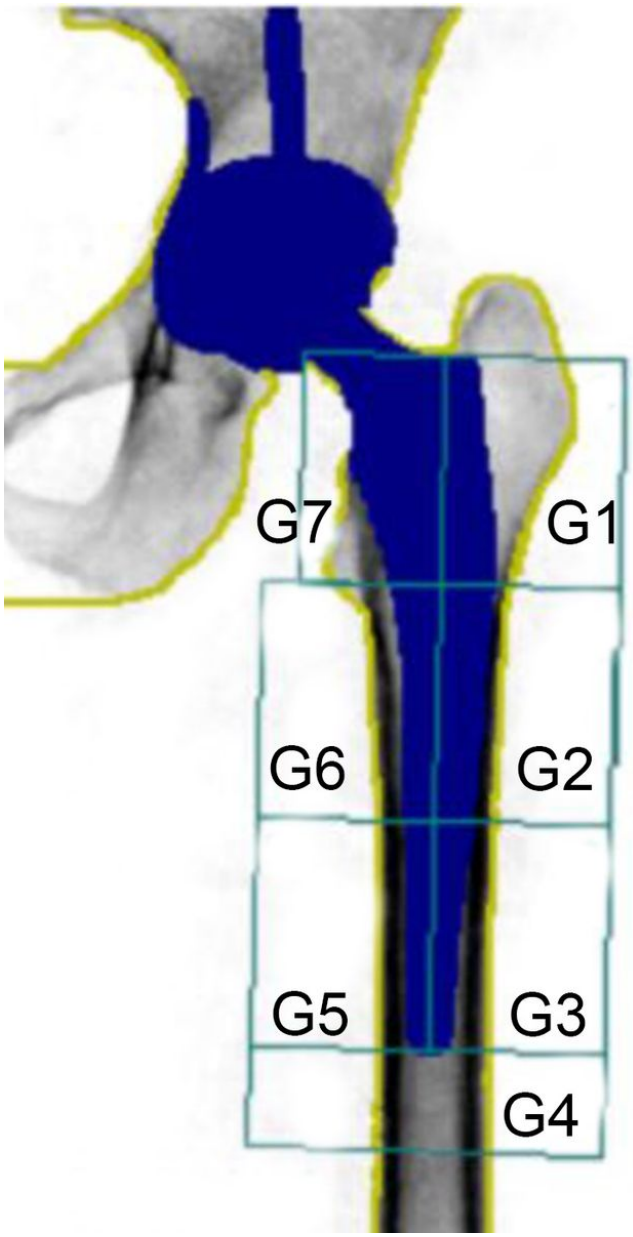

Figure 1

Seven Gruen zones used in Dual-energy X-ray absorptiometrical analysis of postoperative periprosthetic BMD.

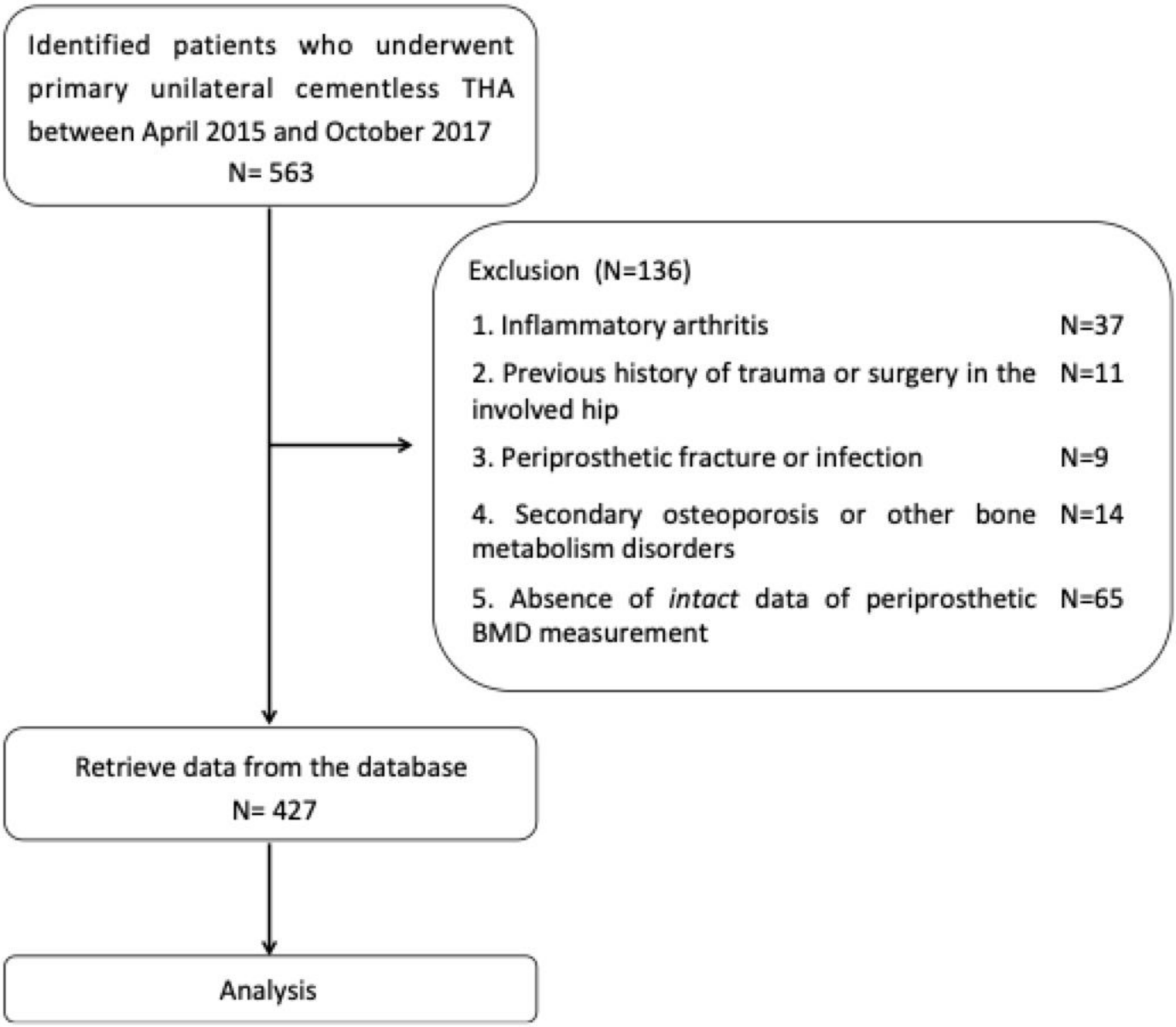

Figure 2

Flowchart.

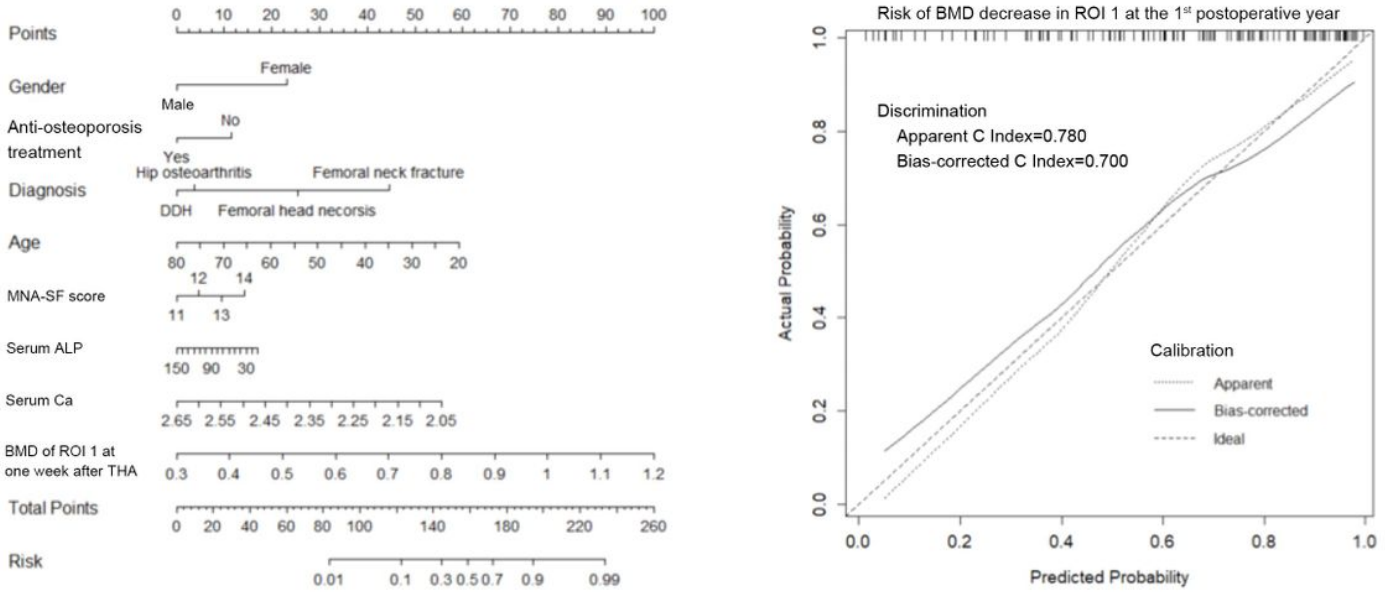

Figure 3

Nomogrampredicting modelforrisk of postoperative bone lossin Gruen zone 1 and the predictionmodelperformance.

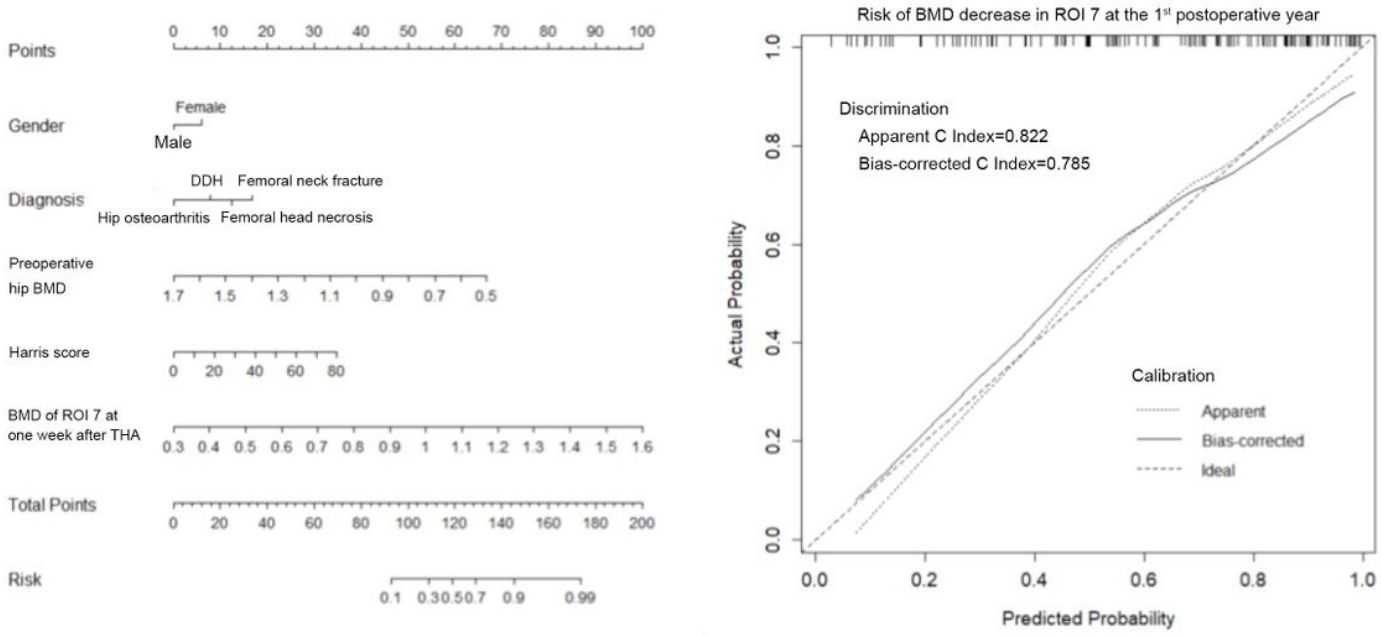

Figure 4

Nomogrampredicting modelforrisk of postoperative bone lossin Gruen zone 7 and the predictionmodelperformancemeasurement.

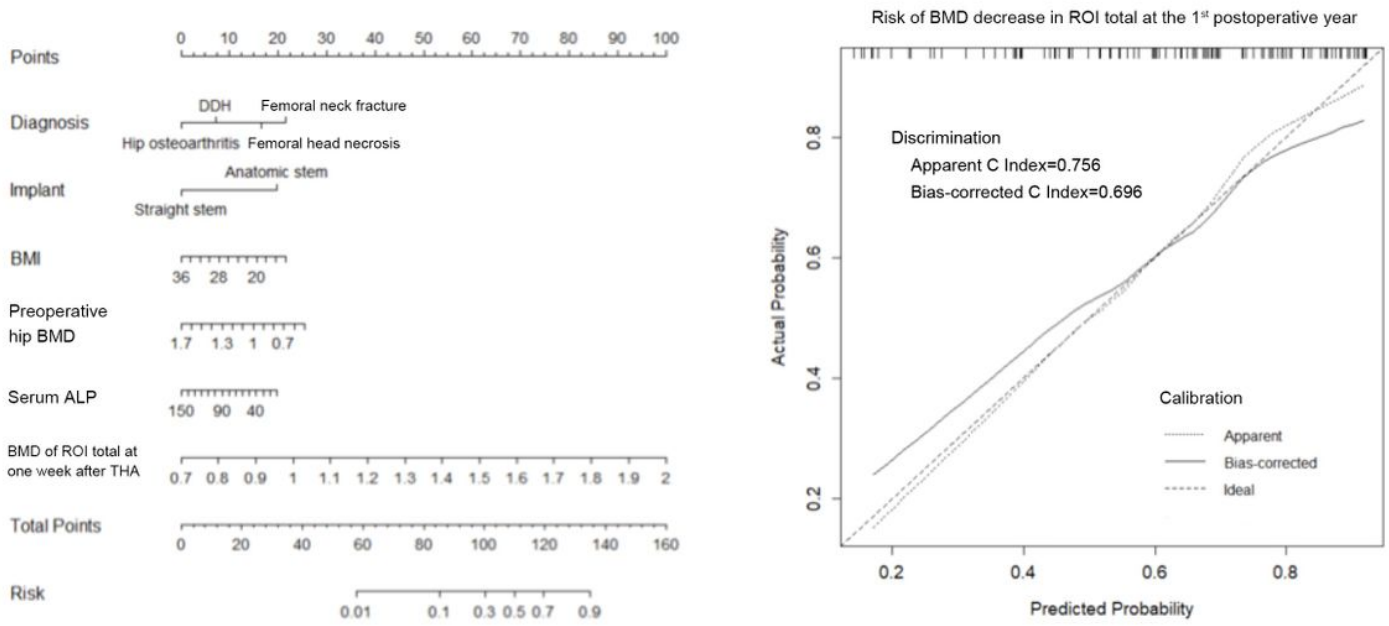

Figure 5

Nomogrampredicting modelforrisk of postoperative bone lossin Gruen zone total and the predictionmodelperformancemeasurement.

Supplementary Files

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- completedTRIPODchecklist.docx