Journal of Hip Preservation Surgery, 2023, **10**, 244–252
DOI: https://doi.org/10.1093/jhps/hnad035
Advance access publication date: 16 October 2023
Review article

Prognosis and risk prediction of bone impaction grafting through femoral head–neck fenestration: a retrospective cohort study

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ABSTRACT

The bone impaction grafting through femoral head–neck fenestration was a favorable hip preservation procedure but without prognosis estimation. This study retrospectively reviewed 79 patients' clinical data (114 hips) with osteonecrosis of the femoral head (ONFH) who underwent this procedure from June 2009 to June 2019. By the end of June 2022, the median survival time of the hip was (74.13 ± 44.88) months, and the success rate of hip preservation was 68.42%. Lateral reserved angle (LPA) and combined reserved angle (CPA) had statistically significant differences ($P < 0.001$) both in univariate analysis and a multivariate logistic regression model. The multivariate logistic regression model of area under curve (AUC) area of the receiver operating characteristic (ROC) curve was 0.931(sensitivity = 95.00%, specificity = 88.40%, log-rank test: $P < 0.01$), and the calibration curve indicated good prediction accuracy. The ROC analysis and Cox proportional hazards regression model revealed that the cutoff point of LPA was 50.95° (sensitivity = 95.00%, specificity = 72.09%, log-rank test: $P < 0.05$) and the cutoff point of CPA was 90.51° (sensitivity = 90.00%, specificity = 90.70%, log-rank test: $P < 0.05$). A nomogram plot to predict the risk of failure (C-index = 0.873, 95% CI: 0.785 to 0.961) and nomograms for predicting the survival probability at 1, 2 or 3 years whose calibration curves showed excellent prediction accuracy were available for the clinician. Preserved angles (PAs) are valuable in the prediction of prognosis in surgical treatment. The bone impaction grafting through femoral head–neck fenestration can achieve better clinical efficacy, especially for patients with LPA >50.95° and CPA >90.51°.

INTRODUCTION

Osteonecrosis of the femoral head (ONFH) is a prevalent and debilitating disease in which the blood supply of the femoral head is damaged or interrupted, resulting in degeneration and necrosis of bone cells and marrow components, and inadequate self-repair of the body triggering collapse, pain and dysfunction of the femoral head [1]. The disease occurs primarily in patients aged 30–50, with insidious onset, rapid progression and a high disability rate [2, 3]. Once progressing to an advanced stage of ONFH, total hip arthroplasty (THA) will ultimately be the inevitable treatment option [4–6]. Due to the complications of THA and the deficiencies of prosthesis durability, hip preservation surgery in the early stages of ONFH to preserve the femoral head and delay initial arthroplasty has high clinical and social value for young and middle-aged patients [7–10].

The bone impaction grafting through femoral head–neck fenestration was a favorable hip preservation procedure [8], which was used for ONFH with a relatively large range of necrotic lesions and mild collapse frequently to achieve adequate decompression, to improve blood flow and to induce osteogenic regeneration by bone grafting [11] under direct vision through head–neck fenestration combining with vascularization procedures like sartorius bone or greater trochanteric bone flap grafting if necessary [12]. Several hip preservation teams have reported the efficacy of this procedure, and the success rate of hip preservation had significant differences in cases with different stages and classifications [8]. Therefore, it is essential to establish an effective and quantitative tool to predict the efficacy of hip preservation based on clinical data preoperative to differentiate whether the patient is suitable for hip preservation treated through this procedure to improve the success rate of hip preservation and the satisfaction of both doctors and patients and to reduce the investment of medical resources.

In this study, we retrospectively analyzed the clinical data of patients treated by bone impaction grafting through femoral head–neck fenestration and the factors affecting the efficacy from multiple perspectives for an effective and quantitative tool to predict the prognosis of hip preservation by artificial

Submitted 16 May 2023; Revised 22 August 2023; revised version accepted 18 September 2023

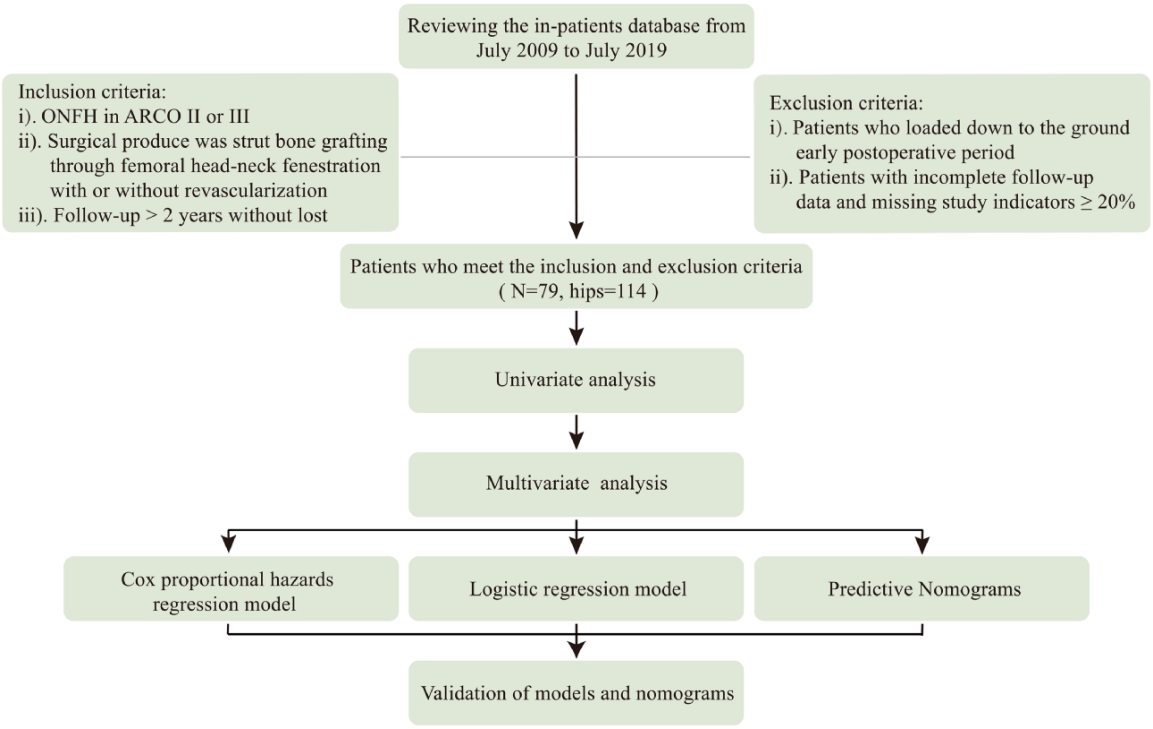

Fig. 1. Flowchart of the study.

machine learning method. The predictive value of the screened key factors may provide a reference for the prognosis of the subsequent clinical application of this procedure for hip preservation.

MATERIALS AND METHODS

Patients

A retrospective study of patients with ONFH who underwent bone impaction grafting through femoral head–neck fenestration from July 2009 to July 2019 was conducted (Fig. 1). The ethics committee of Affiliated Hospital of Nanjing University of Chinese Medicine approved this study and waived the requirement for individual consent. Inclusion criteria: (i) Association Research Circulation Osseous (ARCO) stage of patients was stage-II or stage-III according to the 2019 ARCO staging standards; (ii) follow-up >2 years without lost; (iii) all patients treated with using the same standard surgical technique and postoperative rehabilitation instructions and (iv) all operations were performed by a single, experienced surgeon (Bin Du). The exclusion criteria were as follows: (i) patients who didn't follow medical advice and load down to the ground early postoperative period and (ii) cases with incomplete follow-up data and missing study indicators ≥20%. Diagnostics of imaging staging and necrotic lesions and the measurements of imaging angles were made by two senior orthopedic surgeons in a blinded manner for reliability. If the error of imaging angle measurements varied slightly, the average of the two results was taken. Otherwise, the measures would be re-measured.

Inclusion and pre-processing of indicators

In this study, demographic information, physicochemical testing indexes and imaging indexes which were reported in previous studies [13–16] to be associated with ONFH were recorded. The clinical data of bilateral hip treated by this procedure were recorded twice in the unit of the hip. Indicators with a missing rate <20% would be filled by Multiple Imputation. The measurement data conforming to Gaussian distribution would be expressed as $\bar{x}\pm s$. Otherwise, the data would be described as M (Q1, Q3).

THA or hip with severe pain and limitation of motion, postoperative Harris scores <90 and the progressive collapse of the femoral head on imaging were defined as failure. The

Table I. ***Demographic and clinical characteristics of 79 patients with 114 hips***

Parameter	*Value*
Mean age at initial diagnosis, mean ± SD, years	37.00 ± 10.87
Gender (Male: Female, *n*)	60:54
Affected hip (Left: Right, *n*)	52:62
Onset of symptom, M (Q1, Q3), month	3.00 (2.00, 6.00)
Harris scores (mean ± SD)	67.00 ± 9.62
Etiology, hips, *n*	
Steroid	60
Alcohol	21
Trauma	5
Idiopathic	28
ARCO stage, hips, *n*	
Stage-II	75
Stage-IIIA	31
Stage-IIIB	8
JIC classification, hips, *n*	
Type-C1	79
Type-C2	35

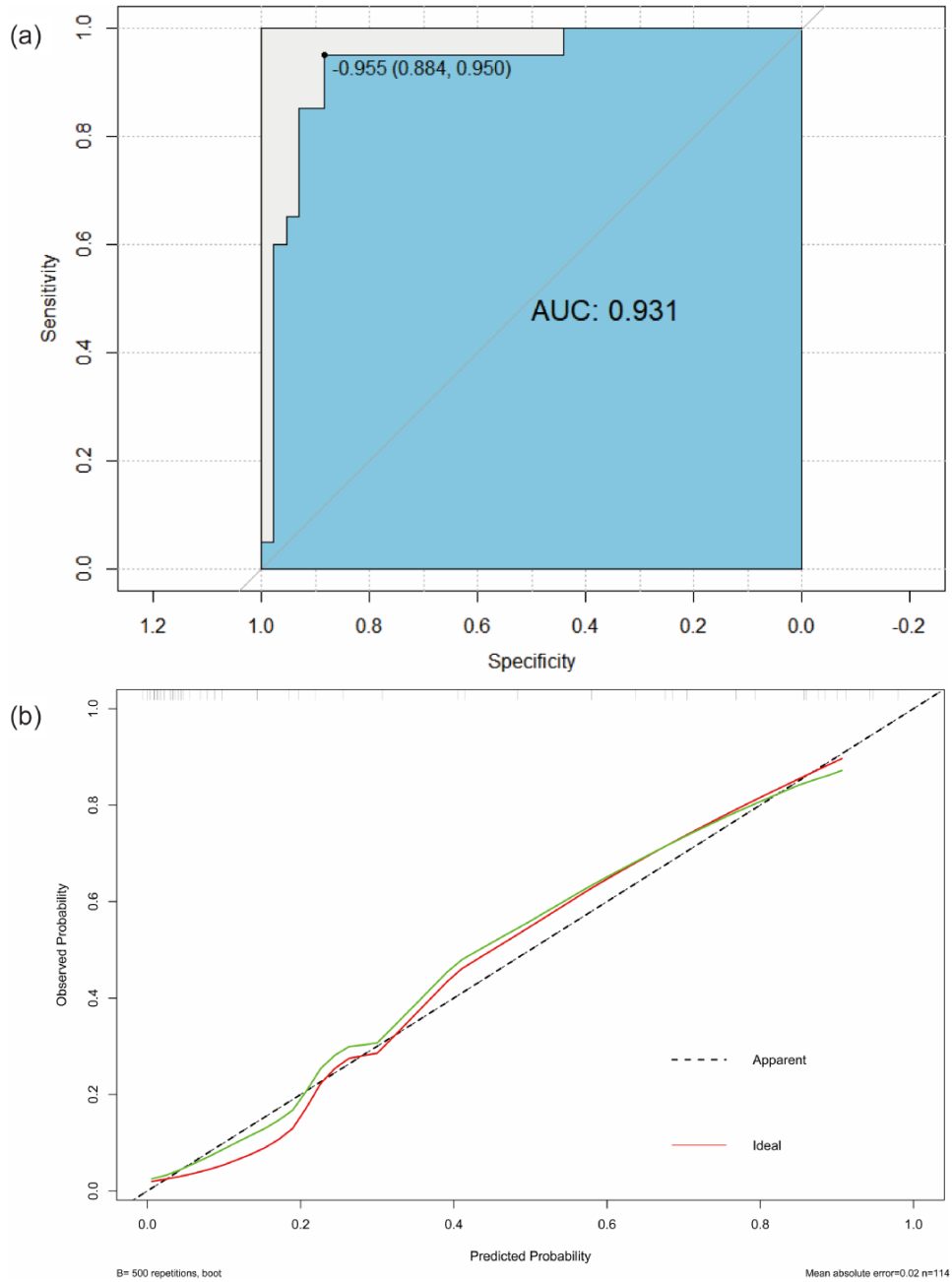

Fig. 2. ROC and calibration curve of multivariate logistic regression model.

patients were divided into a hip preservation success group and a hip preservation failure group based on follow-up in June 2022.

Construction and validation of models

The initial screening of univariate analysis was performed for each indicator between the two groups. Independent sample *t*-test, χ^2 test or Mann-Whitney U test would be appropriately applied for the measurement and enumeration data. The variables with $P < 0.1$ were incorporated into multivariate analysis. Referring to the follow-up results in June 2022 as the dependent variable, a multivariate logistic regression analysis was conducted using forward logistic regression (forward LR) to establish a predictive model for the efficacy. The performance of the model was validated by sensitivity, specificity, a receiver operating characteristic (ROC) curve and area under curve (AUC), calibration curve using bootstrapping with 500 resamples as well.

Defining June 2022 as the follow-up endpoint and hip preservation failure as the survival endpoint, a ROC curve was performed with the aim of defining the cutoff points via selected variables with statistical differences, and Youden's index range was used to assess the performance of these diagnostic thresholds. Predictive nomograms were plotted to predict the risk of failure and the survival probability.

Table II. ***Univariate analysis of various indicators between groups***

Variables		*Group*		$X^2/Z/T$	*P*
		Success (n = 78)	*Failure (n = 36)*		
Gender (*n*)	Male	38	22	*0.586*	*0.444*
	Female	40	14		
Affected side (*n*)	Left	41	11	*0.004*	*0.952*
	Right	37	25		
Etiology (*n*)	Steroid	39	21	*4.145*	*0.246*
	Alcohol	17	4		
	Trauma	4	1		
	Idiopathic	18	10		
Exposure (*n*)	No	66	9	*6.190*	***0.013***
	Yes	12	27		
ARCO stage (*n*)	Stage-II	57	18	*0.357*	*0.836*
	Stage-IIIA	18	13		
	Stage-IIIB	3	5		
JIC classification (*n*)	Type-C1	64	15	*9.898*	***0.002***
	Type-C2	14	21		
Vascularized (*n*)	No	38	20	*0.739*	*0.390*
	Yes	40	16		
Age (years, mean ± SD)		37.10 ± 11.50	36.75 ± 9.66	*0.166*	*0.868*
BMI (kg/m^2, mean ± SD)		22.59 ± 3.29	22.28 ± 3.12	*0.356*	*0.723*
Harris hip score (points, mean ± SD)		68.16 ± 9.51	64.25 ± 9.54	*1.519*	*0.134*
NE (×10^9/L, mean ± SD)		4.35 ± 1.36	3.99 ± 1.52	*0.944*	*0.349*
N (%, mean ± SD)		62.33 ± 9.55	62.47 ± 9.16	*0.055*	*0.957*
ALP (U/L, mean ± SD)		92.12 ± 28.85	83.50 ± 29.49	*1.145*	*0.252*
APA (°, mean ± SD)		66.14 ± 18.32	39.36 ± 15.31	*9.333*	***<0.001***
LPA (°, mean ± SD)		63.43 ± 15.31	28.52 ± 9.76	*5.673*	***<0.001***
CPA (°, mean ± SD)		129.57 ± 23.85	67.88 ± 18.82	*10.173*	***<0.001***
AFU [U/L, M (Q1, Q3)]		16.80(12.60, 20.20)	15.25(12.18, 17.75)	*1.100*	*0.271*
DD [mg/L, M (Q1, Q3)]		0.39(0.28, 0.54)	0.39(0.28, 0.46)	*0.148*	*0.882*
Onset of symptom [months, M (Q1, Q3)]		4.00 (2.00,6.00)	2.00 (2.00,6.00)	*0.907*	*0.364*

Table III. ***Multivariate analysis of various indicators***

Variables	*B*	*Ward*	*P*	*OR*	***95% confidence interval of OR***	
					Lower limit	*Upper limit*
Exposure	*−0.899*	*0.393*	*0.531*	*0.407*	*0.025*	*6.759*
JIC classification	*−2.179*	*2.179*	*0.140*	*0.113*	*0.006*	*2.043*
APA	*−0.054*	*0.950*	*0.330*	*0.948*	*0.851*	*1.056*
LPA	*−0.205*	*6.407*	***0.011***	*0.815*	*0.695*	*0.955*
CPA	*−0.128*	*9.165*	***0.002***	*0.880*	*0.810*	*0.956*
Constant	*−0.765*	*7.999*	*0.005*	*0.465*		

Table IV. ***AUC of the ROC curve***

	Area	*Std. Error*	*P value*	*95% confidence interval*		*Cutoff value*	*Youden's Index*
				Lower limit	*Upper limit*		
LPA	0.904	0.037	<0.001	0.831	0.978	50.95	0.671
CPA	0.921	0.033	<0.001	0.871	0.984	90.51	0.807

Statistical analysis

All statistical analyses were performed using SPSS (version 26.0, IBM, USA), GraphPad Prism (version 8.0, GraphPad, San Diego, CA, USA), R statistical software (version 4.1.2, Institute for Statistics and Mathematics, Vienna, Austria) and RStudio software (version 1.2.5042, RStudio, Boston, USA). We used the 'MASS' package and 'lrm' package for the construction and validation of the multivariate logistic regression model, and plotting

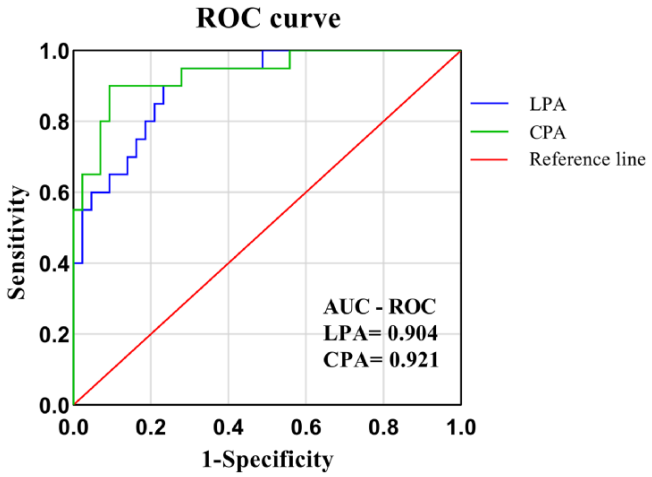

Fig. 3. ROC curve of LPA and CPA.

The ROC revealed that the LPA and CPA had a good ability to predict prognosis with high sensitivity. The cutoff point of LPA was 50.95° (sensitivity = 95.00%, specificity = 72.09%) and the cutoff point of CPA was 90.51° (sensitivity = 90.00%, specificity = 90.70%).

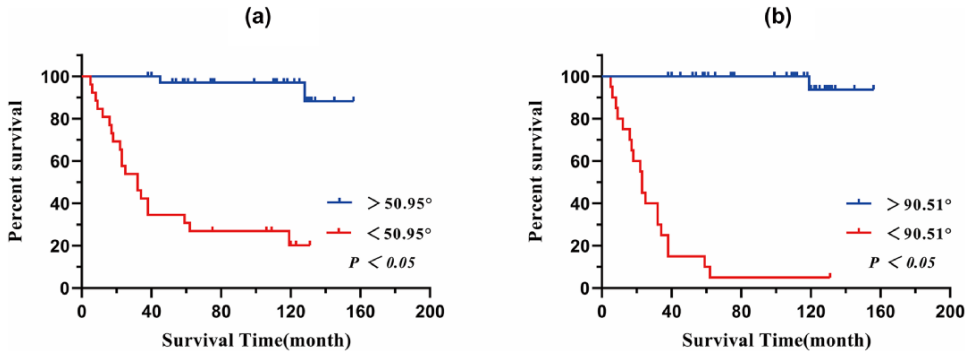

Fig. 4. Cox survival regression based on cutoff point of LPA and CPA.

Cox survival regression was constructed based on LPA's (Fig. 4A) and CPA's (Fig. 4B) cutoff point.

of ROC curves was accomplished using the 'pROC' package. The construction of nomograms and Cox survival regression were performed by the 'rms' packages. C-index and calibration curve using bootstrapping with 1000 resamples by the 'hdnom' package were accomplished to assess the nomograms. All statistical analyses were two-sided and evaluated with a $P < 0.05$ used to indicate statistical significance.

RESULTS

General information

Between July 2009 and July 2019, 79 patients with 114 hips were treated by bone impaction grafting through femoral head–neck fenestration and included in this study. Their demographic and clinical characteristics are shown in Table I.

Analysis of influencing factors and model validation

By the end of June 2022, the median survival time of the hip was 74.13 ± 44.88 months. Seventy-eight hips had a satisfactory curative effect without THA, poor hip function or progressive collapse of the femoral head on imaging, and the success rate of hip preservation was 68.42%. Comparing various indicators between groups, we found that exposure to risk factors postoperative, Japanese Investigation Committee (JIC) classification, lateral reserved angle (LPA) and combined reserved angle (CPA) had significant statistical significance ($P < 0.001$), which may be the influencing factors of the curative effect of hip preservation (Table II). The indicators above were incorporated into multivariate logistic regression analysis, and LPA and CPA had statistically significant differences ($P < 0.05$) (Table III). According to the validation of the data, the multivariate logistic regression model of AUC was 0.931(sensitivity = 95.00%, specificity = 88.40%, log-rank test: $P < 0.01$); meanwhile, the calibration curve indicated good prediction accuracy (Fig. 2A and B).

Cox regression model and predictive nomogram

LPA and CPA's predictable value was demonstrated by survival analysis (Table IV). The ROC curves based on LPA and CPA are presented in Fig. 3. The ROC analysis revealed that the cutoff point for the LPA was 50.95° (sensitivity = 95.00%, specificity = 72.09%, log-rank test: $P < 0.05$). The cutoff point for the CPA was 90.51° (sensitivity = 90.00%, specificity = 90.70%, log-rank test: $P < 0.05$). Cox proportional hazards regression model was constructed based on the cutoff point above with hip preservation failure as the survival endpoint (Fig. 4A and B).

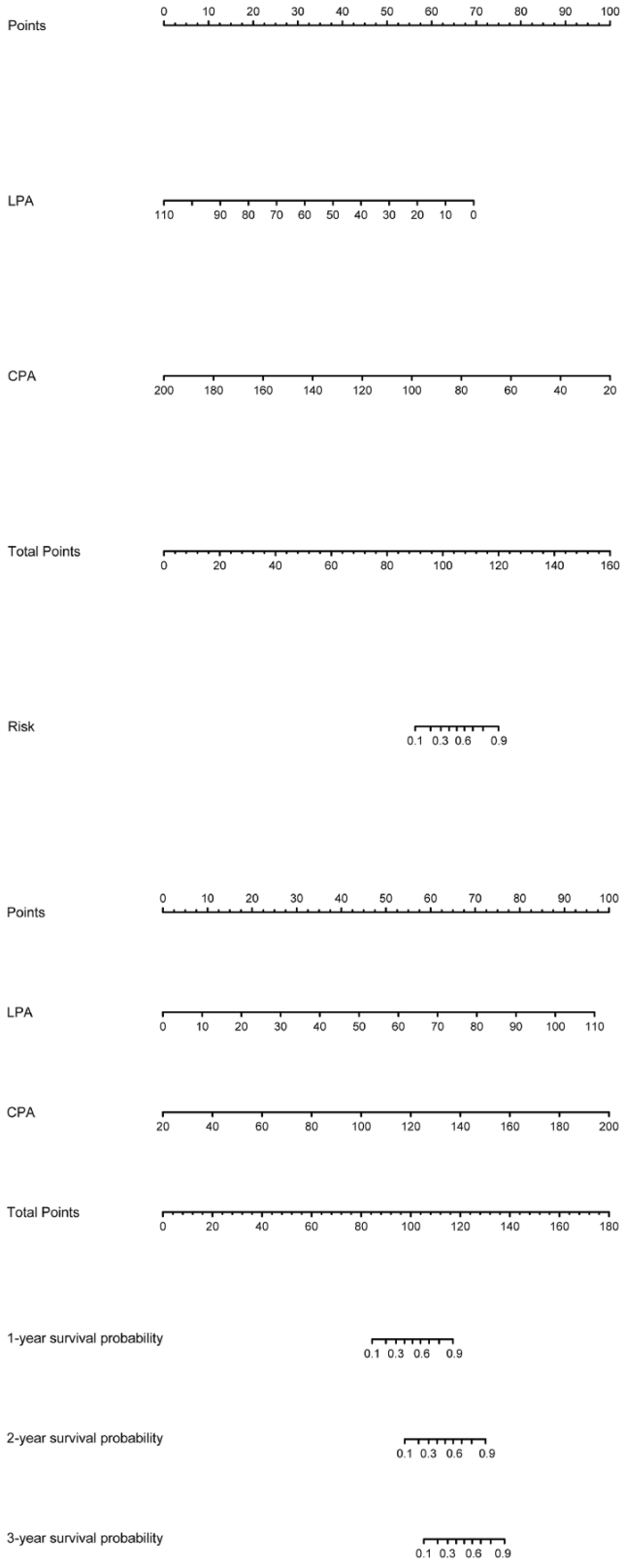

Fig. 5. Nomogram for predicting the risk of failure and survival probability.

The study used two independent risk factors for hip preservation failure and 1, 2, 3 year survival probability after bone impaction grafting through femoral head–neck fenestration to make nomograms; their scores could indicate significant positive and negative correlations and the importance of the factors.

To provide the clinician with a quantitative tool to predict the risk of failure and the survival probability, predictive nomograms were built based on multivariable analysis (Fig. 5). After the internal validation, the C-index of the nomogram to predict the risk of failure was 0.873 (95% CI, 0.785 to 0.961), which had excellent prediction accuracy. The calibration curves for predicting the survival probability at 1, 2 or 3 years after surgery of each model after 1000 times of bootstraps are shown in Fig. 6, and they show similarly good agreement between the estimation and actual observation. According to the nomograms, the higher LPA and CPA will significantly decrease the risk of failure and improve the survival probability.

DISCUSSION

The concept of preserved angles (PAs) was first proposed by Wei *et al.* [17]. They found that the PAs, specifically CPA on plain radiographs, had a potential value in predicting femoral head collapse by assessing the angles in patients with ONFH treated conservatively. We conducted a retrospective study of patients treated by bone impaction grafting through femoral head–neck fenestration to evaluate the value of PAs for the prediction of efficacy in surgical treatment and to achieve a predictive model for identifying the indications of this procedure as well.

The extent and location of necrosis of the femoral head are recognized factors of prognosis of the femoral head [18], and the integrity of the anterolateral column plays a vital role in maintaining the function of the femoral head [19, 20]. Previous studies had concluded that patients with necrosis of <30%, confined to the middle of the femoral head and collapse of <2 mm could have better efficacy of hip preservation [8, 21, 22]. In this study, JIC classification had statistical significance, which reflected the extent of necrosis and the degree of involvement of the lateral column. However, to the best of the authors' knowledge, the currently prevailing international staging and classification, including ARCO stage and JIC classification, can't describe the extent of anterior femoral head involvement accurately [23–25]. The PAs proposed by Wei *et al.* described both the anterior and lateral involvement of the femoral head, and non-operative treatment can be accepted when the CPA is greater than 118°. On the contrary, when the CPA is less than 118°, surgical treatment should be considered to preserve the hip [17]. In this study, we found that hip preservation was more effective when the CPA was greater than 90.51° with bone impaction grafting through femoral head–neck fenestration.

Compared with conservative treatment, bone impaction grafting through femoral head–neck fenestration can expose most of the femoral head, allow the operator to remove the dead bone in the head and fill it with autologous or allogeneic bone under direct vision. It provides sufficient mechanical support and osteogenic matrix in the head, reducing the effect of intracranial pressure and offering conditions for vascular ingrowth [8, 26]. To some extent, the procedure supports the partially collapsed femoral head and reconstructs or strengthens the anterolateral column. However, it is worth noting that although this procedure has the advantage of being able to perform thorough debridement of dead bone, the massive removal of necrotic bone, especially within the anterolateral column, may reduce

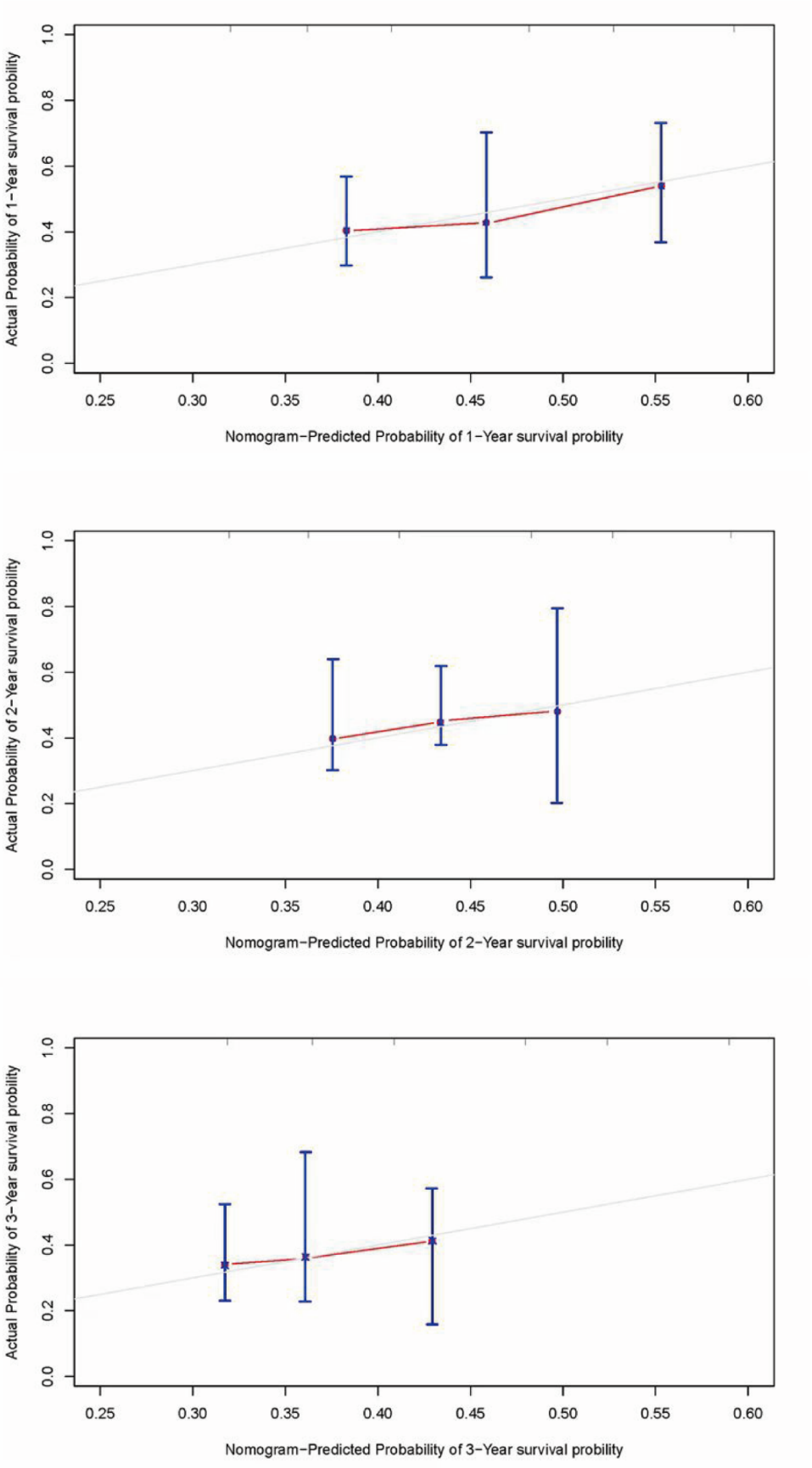

Fig. 6. The calibration curves of the nomograms for predicting the survival probability at 1, 2 or 3 years.

the mechanical stability of the femoral head to some degree. For patients with an extensive necrotic range, especially with CPA <90.51°, the increase in the range of fenestration will cause more severe damage to the articular cartilage, increasing the risk of hip preservation failure. The surgeon should consider and select the appropriate patient to ensure that both the doctor and the patient benefit.

This study is limited by its retrospective single-center design and the relatively small patient cohort, resulting in a small sample size and possible bias. For example, both vascularized and non-vascularized bone grafting are commonly performed surgical procedures for the management of ONFH [27, 28], but there is still some controversy regarding the efficacy of them. Some studies [29, 30] suggest that vascularized bone grafting is associated with better clinical and radiographic outcomes. However, we did not find a relationship between vascularized bone grafting and efficacy of hip preservation in this study, which may be related to the sample size. Furthermore, some indicators, such as blood lipids and cholesterol, which were reported to be associated with ONFH [31], were not included in the study due to excessive missing rates. They may have some influence on the credibility of the study. Therefore, expanding the sample size, extending the follow-up period and integrating more variables could be considered in future studies.

CONCLUSIONS

PAs are valuable in predicting prognosis in surgical treatment. The bone impaction grafting through femoral head–neck fenestration can achieve better clinical efficacy, especially for patients with LPA >50.95° and CPA >90.51°.

AVAILABILITY OF DATA AND MATERIALS

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

ACKNOWLEDGEMENTS

We would like to express our sincere gratitude to all the patients who participated in this study.

FUNDING

This work was supported by the National Natural Science Foundation of China (grant No.82074471).

CONFLICT OF INTEREST STATEMENT

None declared.

CONSENT FOR PUBLICATION

All authors have seen the article and approved it to submit to your journal.

NOTES ON CONTRIBUTORS

Hao Chen was responsible for data analysis and article writing. Shuai He contributed to data collection and follow-up. Hongzhong Xi organized, reviewed and illustrated the research process. Peng Xue was responsible for data statistics. Bin Du contributed to the language editing. Xin Liu was responsible for the study design and correspondence. All authors read and approved the final article.

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