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Research Article

A Web-Based Dynamic Nomogram to Calculate the Risk of Nonhealing after Femoral Neck Fracture Fixation among Young Adults: Bench to Bedside Translational Research

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Abstract

Background: The aim of this study was to develop a prognostic model to identify a subgroup of high-risk patients for non-healing after femoral neck fracture fixation among young adults. The model was implemented by presenting graphically as a nomogram that could be easily used in every day clinical cases.
Methods: Data on a total of 129 patients were included in the current study. The mean [standard deviation (SD)] age of the participants was 42 (13) years and 28% of the patients were women. Harrell's C statistic was used as a measure of discrimination predictive power. We calculated the Nam-D'Agostino χ^2 to examine calibration for prediction models.
Results: Approximately, 83% of fractures united uneventfully, with avascular necrosis (AVN), fixation nonhealing, non-union, infection, arthroplasty, and death being observed. Body mass index (BMI) and head acetabular trabecular angle (HATA) were inversely associated with the risk of all-cause nonhealing. The final model showed excellent discriminatory power [Harrell's C statistic: 0.820, 95% confidence interval (CI) (0.680-0.960)] and it was well-calibrated [Nam-D'Agostino χ^2: 10.1, (P = 0.3456)]. A nomogram developed by incorporating significant predictors modelled without discretizing continuous variables.
Conclusion: Using readily available clinical and radiological data, we developed a parsimonious, simple, accurate yardstick to measure the 5-year risk of nonhealing after femoral neck fractures among young adults. In order to add ease-of-use and to promote its integration into clinical practice, the prognostic model was demonstrated visually as a statistic nomogram.

Keywords: Femoral Neck Fracture; Nomograms; Risk

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Background

Hip fractures, which have been the objective of many studies for many years, commonly lead to premature death, high rates of morbidity, or reduced quality of life (QOL) (1). The vast majority of hip fractures occur in the elderly population as a result of osteoporosis and in association with simple falls (2). The 1-year mortality among elderly patients with hip fracture has been reported as 20-30 percent (2-10). In contrast, hip fractures among young adults, in who it is uncommon, is generally caused by high-energy trauma (11-20). In North America, less than 10% of hip fractures occur among young adults younger than 60 years of age (2). The survival rate of hip fracture among young adults is > 90% (12-17, 19, 20). Few studies have recently investigated the outcomes of hip fractures among young adults (11-20). However, there was a lack of evidence on the long-term outcomes of hip fractures in young Middle Eastern adults. Given the rarity of complications in the era of modern orthopedic surgery, the number of nonhealing was few in the vast majority of studies, so it is difficult to identify statistically significant variables leading to nonhealing (18). Accordingly, this study aimed, primarily, to increase our knowledge on the rates of complications in hip fracture among young adults and its risk factors. An attempt was also made to identify a subgroup of patients at high risk for developing complications where close observation and preparedness might be warranted. The prognostic model has been presented graphically as a nomogram that could easily be utilized in the everyday clinical encounters. A web-based calculator has also been developed for estimating the risk of nonhealing.

Methods

Participants: The study population included patients with femoral neck fracture referred to a large tertiary trauma center, during 2012-2018. For the current analysis, we included patients treated with dynamic hip screw (DHS) fixation, for whom medical records were available for the variables under investigation. Data of 129 patients were included in the current analysis. The mean [standard deviation (SD)] age of the participants was 42 (13) years and 28% of the patient were women.

Exposures: The patients were followed up with the first postoperative visit being scheduled 2 weeks after the index operation when sutures were generally removed. Usually,

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the patients were further evaluated at 6 and 12 weeks and 6, 12, and 24 months after surgery. At each and every follow-up visit, a pelvic anterior-posterior (AP) and a lateral hip x-ray was obtained.

Study Outcome: The occurrence of any of the following events was considered nonhealing. Instead of evaluating cause-specific nonhealing, we examined nonhealings from any causes (nonhealing) to increase the statistical power of the regression models.

1. Event-free union
2. Nonunion
3. Infection
4. Device nonhealing
5. Arthroplasty
6. Death
7. Avascular necrosis (AVN) of the femoral head

Measurements: Using a predetermined questionnaire, we gathered data on age, sex, body mass index (BMI), smoking, alcohol use, opium abuse, past medical history of rheumatologic diseases, and mechanism of trauma.

Preoperative radiographic examinations were studied by the first author and following indices were measured and recorded using a picture archiving and communication system (PACS) calibrated for magnification.

1. Pauwels angle
2. Postoperative angulation: varus/valgus
3. Preoperative and postoperative translation
4. Garden alignment index (GAI) in AP view
5. GAI in lateral view
6. Dorr score
7. Fracture site
8. Comminution
9. Tip-to-apex distance
10. The position of anti-rotation screw
11. Head-acetabulum trabecular angle (HATA)

Statistical Analysis: Data were presented as either mean (SD) or frequency (%) for continuously- and categorically-distributed variables, respectively.

Our methods for the survival analysis of nonhealing as the outcome were similar to those in an earlier paper (21, 22). Briefly, the association of the candidate potential predictors with nonhealing was assessed using flexible parametric survival regression models (23, 24). Censored observation was defined as the individuals who either refused to participate further in the study (lost to follow-up), died from non-fracture related causes, when mortality was not the outcome (competing risk), or continued to attend the follow-up examinations until the study was ended (administrative censoring). The censoring time of an individual was calculated from the date of the index surgery to the end of the study or the date when a participant was lost to follow-up, whichever happened first. The survival time included the time from the start of the follow-up period (date of the index surgery) to the date of the first incident, nonhealing of any cause.

As suggested by Steyerberg et al. (25), predictive performance of the competing prognostic models were assessed in terms of the calibration, discrimination, and added predictive ability (26).

Calibration describes how closely model-based predicted probabilities of nonhealing from any cause agree numerically with actual nonhealing rate observed during the follow-up (27-31). D'Agostino and Nam proposed a test very similar to the Hosmer-Lemeshow test. The Nam-D'Agostino χ^2 was calculated to examine calibration for prognostic models. As suggested by D'Agostino and Nam, calibration χ^2 values greater than 20 ($P < 0.01$) suggest lack of adequate calibration (32).

A statistical index similar to the area under the receiver operating characteristic (ROC) area under the curve (AUC) has been suggested for quantifying the discriminatory power of the survival regression models. In the current survival analysis, Harrell's C statistic indicates the probability that a randomly selected person who developed nonhealing of any cause, at the certain specific time has a higher risk score than a person (selected randomly during the same, specific follow-up interval) who did not develop the event (24, 33).

Discrimination measures have long been known as not being sensitive to changes in absolute risk. We, thus, calculated absolute and relative integrated discrimination improvement (IDI) index and cut-point-based and cut-point-free net reclassification improvement (NRI) index. IDI and NRI were used to measure the predictive ability added to the basic prognostic model by translation. In order to obtain bias-corrected 95% confidence intervals (95% CIs), we implemented the bootstrapping method, with 1000 resampling (34-46).

A potential nonlinear association of continuously-distributed variables with nonhealing was examined by running a series of multivariate fractional polynomials (47-50).

The mathematical formula of prediction algorithm obtained from the flexible survival regression modeling of the significant predictors were incorporated into a nomogram. The nomogram developed herein serves as a graphical representation of our prediction algorithm incorporating significant predictors modeled as continuous variables to predict the risk of nonhealing.

We hereby certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this study. Informed written consent was not obtained from any participants due to the retrospective nature of the study, and the study was approved by the Ethical Committee of Tehran University of Medical Sciences, Tehran, Iran. The investigations reported herein have been carried out in accordance with the principles of the Declaration of Helsinki (DoH) as revised in 2008.

The statistical significance level was set at a two-tailed type I error of 0.05. All statistical analyses were performed using STATA version 16 (STATA, College Station, Texas USA). Nomogram and web-based calculation tools were developed using RStudio (version 1.2.5033 © 2009-2019 RStudio, Inc).

Sensitivity Analysis: We also performed a sensitivity analysis against the backdrop of the argument as the behavior of the candidate potential predictors in contributing to the risk of non-healing femoral neck fracture from different endpoints might have been different. To this end, we repeated all analyses with fixation nonhealing and AVN as the outcome and observed that the results remained essentially the same. As such, in order to abide by the rules of parsimony and to avoid inflation in the type 1 error and multiplicity of inference, we decided to report nonhealing of any cause in combination (data were available upon the request from the authors).

Definitions of Terms

1. Pauwels angle is the angle between the line of fracture of the femur neck and the horizontal line as seen on an AP radiograph. The Pauwels angle is named after the German orthopedist Friedrich Pauwels (51).
2. The GAI, which analyzes the direction of the trabeculae,

indicates the degree of rotation of the femoral head. In the AP projection (GAI_{AP}), the cervicocephalic trabeculae form an angle of 160-175° with the medial cortical bone of the femoral diaphysis; in the lateral projection (GAI_{Lat}), the alignment of the trabeculae should be 180°. From the GAI, adequate reduction is taken to be a trabecular angle of between 160° and 180°, both in AP and in lateral views (52-54).

3. The Tip Apex Distance (TAD) is the sum of the distance from the tip of the screw to the apex of the femoral head on AP and lateral views (55-57).
4. To allow for confounding bias and at the same time avoid over adjustment, we combined the GAI_{AP} and GAI_{Lat} and calculated a Pythagorean GAI as follows:

$$GAI_{Pythagorean} = \sqrt[2]{(180 - GAI_{AP})^2 + (180 - GAI_{Lat})^2}$$

Ethics: We hereby certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this study. Informed written consent was not obtained from any participants due to the retrospective nature of the study, and the study was approved by the Ethical Committee of Tehran University of Medical Sciences. The investigations reported herein have been carried out in accordance with the principles of the DoH as revised in 2008.

Results

Estimation of the Rate of Nonhealing from Any Causes (All-Cause Nonhealing) after Fixation of Femoral Neck Fracture Treated with DHS in Young Adult Patients

Approximately, 83% of fractures united uneventfully, with AVN, fixation nonhealing, nonunion, infection, arthroplasty, and death being observed among 8.5, 6.2, 3.9, 3.9, 10.9, and 1.6% of the participants, respectively. During a median 3-year follow-up period, we documented 22 all-cause nonhealing complicating femoral neck fractures. Using data on 358 person-year follow-ups, the annual complication rate was estimated to be 6.1 per 1000 fractures. BMI and HATA were inversely associated with the risk of all-cause nonhealing. Table 1 shows the baseline characteristics of the participants.

About 17 and 24% of the participants reported alcohol and opium use of varying amounts, respectively. Pauwels types of 1, 2, and 3 were distributed respectively among 19.4, 30.2, and 50.4% of the participants. Dorr classes of 1, 2, and 3 were distributed among 31.8, 51.2, and 17.1% of the participants, respectively. The fracture occurred in subcapital, transcervical, and basicervical area of femoral neck among 31.8, 53.5, and 14.0% of the participants, respectively. More than 28% of the patients underwent open reduction. Commination was observed among 29% of the fractures. Anti-rotation screws were placed in a normal position in 60% of cases with 20 and 16% being placed in anterior and posterior position, respectively.

Table 1. Baseline characteristics of the participants

		Mean	SD	Min	Max
Age (year)	129.0	42.0	13.0	16.0	61.0
BMI (kg/m^2)	129.0	24.6	2.8	18.0	33.0
Head-neck trabecular angle (°)	129.0	30.7	24.6	0.0	100.0
Pauwel angle (°)	129.0	54.0	23.1	12.0	90.0
Postoperative translation (mm)	129.0	2.1	1.5	0.0	6.0
Angulation (°), absolute values	129.0	5.5	5.4	0.0	32.0
Tip-to-apex distance (mm)	129.0	21.2	6.0	9.0	38.0
GAI AP view (°)	129.0	169.3	6.1	154.0	180.0
GAI lateral view (°)	129.0	173.4	16.0	4.0	180.0
postoperative varus angulation (°)	129.0	8.5	4.6	2.0	17.0
postoperative valgus angulation (°)	129.0	4.8	4.5	0.0	19.0
Angle, net values (°)	129.0	-3.3	6.9	-32.0	17.0
Pythagorean combination of Garden indices	129.0	14.4	15.6	1.0	176.0

SD: Standard deviation; BMI: Body mass index; GAI: Garden alignment index

The reduction was obtained in a normal position in 33% of cases with 10 and 57% being obtained in varus and valgus position, respectively. Univariate contribution of the candidate predictors to hazard of all-cause failure is shown in table 2.

Identification of the Fracture-, Patient-, or Treatment - Related Factors that Might Have Contributed to the Risk of All-Cause Nonhealing among Potential Predictors Such As Body Mass Index (BMI), High Impact Energy Trauma, or Reduction Techniques

Table 3 represents the multivariate contribution of candidate predictors to the 5-year risk of all-cause nonhealing after femoral neck fracture fixed with DHS. When association of the potential predictors was adjusted for potential confounding bias imposed by other covariates, BMI [0.29], HATA, translation, malposition of anti-rotation screw, reduction angulation, high impact energy trauma, and open reduction resisted all adjustments. When significant predictors were incorporated into a multivariate model, translation and the position of anti-rotation screw no longer achieved statistical significance.

Table 2. Univariate contribution of the candidate predictors to hazard of all-cause failure

Potential predictors of all-cause failure	HR[1]	95% CI[2]		SE[3]	Z	P
Age (year)	1.11	0.71	1.74	0.25	0.45	0.654
BMI (kg/m^2)	0.75	0.47	1.18	0.17	-1.26	0.207
Smoking (pack/year)	1.06	0.71	1.576	0.22	0.27	0.788
HATA (°)	0.81	0.52	1.26	0.18	-0.93	0.351
Pauwels angle (°)	0.86	0.58	1.28	0.17	-0.74	0.457
Tip-to-apex distance (mm)	1.17	0.76	1.80	0.26	0.73	0.465
Reduction angulation (°)	1.74	1.15	2.613	0.36	2.65	0.008
GAI AP view (°)	0.69	0.49	0.99	0.13	-2.02	0.044
GAI lateral view (°)	0.86	0.72	1.03	0.08	-1.64	0.100
Pythagorean sum of Garden indices	1.20	1.01	1.42	0.10	2.11	0.034
Postoperative translation (mm)	1.32	0.85	2.06	0.30	1.23	0.217
Angulation (°)	1.74	1.15	2.613	0.36	2.65	0.008
Female vs male	1.30	0.53	3.19	0.59	0.57	0.572
Opium abuse	0.76	0.28	2.08	0.39	-0.53	0.599
Past medical history of rheumatologic diseases	1.50	0.63	3.60	0.67	0.91	0.363
Anti-rotation screw not in center-center position	2.28	0.97	5.35	0.99	1.90	0.058
Fracture anywhere vs subcapital	1.27	0.49	3.25	0.61	0.49	0.624
High vs low impact energy trauma	1.54	0.57	4.20	0.79	0.85	0.394
Comminuted fractures vs non-comminuted fracture	1.95	0.84	4.53	0.84	1.56	0.120
Translation vs no translation	2.26	0.53	9.692	1.68	1.10	0.273
Varus reduction	6.37	2.66	15.25	2.84	4.15	0.000
Open reduction vs closed reduction	4.87	2.04	11.65	2.17	3.56	0.000

HR: Hazard ratio; for continuously distributed variables reported for a 1-SD increment; CI: Confidence interval; SE: Standard error; BMI: Body mass index; HATA: Head-acetabulum trabecular angle

Table 3. Multivariate contribution of the candidate predictors to the hazard of all-cause failure

Potential predictors of all-cause failure	HR[1]	95% CI[2]		SE[3]	Z	P
Age (year)	0.95	0.42	2.16	0.40	-0.12	0.901
BMI (kg/m^2)	0.29	0.12	0.73	0.14	-2.64	0.008
Smoking (pack/year)	1.93	0.74	5.03	0.94	1.34	0.180
Head-neck trabecular angle (°)	0.44	0.19	0.98	0.18	-2.00	0.046
Pauwels angle (°)	1.04	0.52	2.10	0.37	0.11	0.911
Tip-to-apex distance (mm)	0.92	0.43	1.94	0.35	-0.23	0.822
Reduction angulation (°)	0.28	0.09	0.86	0.16	-2.22	0.026
GAI AP view (°)	0.40	0.07	2.33	0.36	-1.02	0.307
GAI lateral view (°)	0.18	0.00	12.73	0.39	-0.79	0.431
Pythagorean sum of Garden indices	0.31	0.01	17.17	0.64	-0.57	0.571
Postoperative translation (mm)	0.86	0.31	2.42	0.45	-0.28	0.777
Absolute reduction angulation (°)	0.26	0.07	1.03	0.18	-1.92	0.055
Female vs male	1.67	0.29	9.65	1.49	0.57	0.569
Opium abuse	0.58	0.08	4.13	0.58	-0.54	0.590
Past medical history of rheumatologic diseases	0.42	0.07	2.39	0.37	-0.98	0.328
Anti-rotation screw not in normal position	5.67	1.05	30.64	4.88	2.02	0.044
Fracture anywhere vs subcapital	2.41	0.28	20.60	2.64	0.80	0.423
High vs low impact energy trauma	5.94	0.73	48.49	6.36	1.66	0.096
Comminuted fractures vs non-comminuted fracture	0.56	0.13	2.32	0.40	-0.81	0.420
Translation vs no translation	2.81	0.13	58.87	4.36	0.67	0.505
Varus reduction	40.26	1.83	885.73	63.49	2.34	0.019
Open reduction vs closed reduction	13.25	2.21	79.51	12.11	2.83	0.005

HR: Hazard ratio; for continuously distributed variables reported for a 1-SD increment; CI: Confidence interval; SE: Standard error; BMI: Body mass index; HATA: Head-acetabulum trabecular angle

Table 4 shows the hazard ratio (HR) (95% CI) for variables that rested all adjustments and incorporated into the final basic parsimonious model including: BMI [0.32 (0.16-0.64))], HATA [0.49 (0.26-0.94)], high impact energy trauma [3.55 (0.1.08-11.7)], varus reduction [8.56 (2.39-30.57)], and open reduction [4.96 (1.69-14.59)]. Although the hazard ratio for all-cause nonhealing of the translation did not achieve statistical significance [HR: 2.56 with 95% CI (0.51-13.69), P = 0.245], we preferred to retain it in the final prognostic model, because it added to predictive value of the final parsimonious model. We here refer to the model incorporating translation as an improved prognostic model.

Development and Validation of a Prognostic Model Using Simple Clinical and Readily Available Radiologic Information to Predict the Risk of Nonhealing of Femoral Neck Fractures among Young Adults Treated with DHS

Table 5 compares the predictive power of the prognostic models in terms of discriminative capacity, calibration, explained variation in the outcome of interest (nonhealing-free survival time), and the predictive ability conferred by adding translation to the baseline model. Figure 1 graphically presents how well the estimated risk of nonhealing from the flexible survival regression modeling of significant predictors are in agreement with the nonhealing rate observed from the Kaplan-Meier estimator. The final model was well-calibrated [Nam-D'Agostino χ^2: 10.1, (P = 0.3456)] and it showed an excellent discriminatory power [Harrell's C statistic: 0.820, 95% CI (0.680-0.960)]. As shown in table 5, adding translation to the baseline model improved the predictive power of the prognostic model. More than 50% of the participants were reclassified appropriately when the information on the presence of translation after reduction of their fracture was taken into account [cut-point-free NRI: 0.55 (0.03-1.08), P = 0.040)].

Graphical Presentation of the Developed Prognostic Model as a Nomogram that Could Easily be Utilized in Everyday Clinical Encounter and Development of a Web-based Calculator for Estimating the Risk of Nonhealing

The prognostic model is graphically demonstrated as a nomogram (Figure 2) that could be easily used without any advanced knowledge of statistics (available at: https://rpubs.com/mhmmdrz_bzrgmnsh/607332). Second, the nirvana of simplicity is achieved by few clicks on the website: https://drbozorgmanesh.shinyapps.io/DynNomappFNFxPrognostication/.

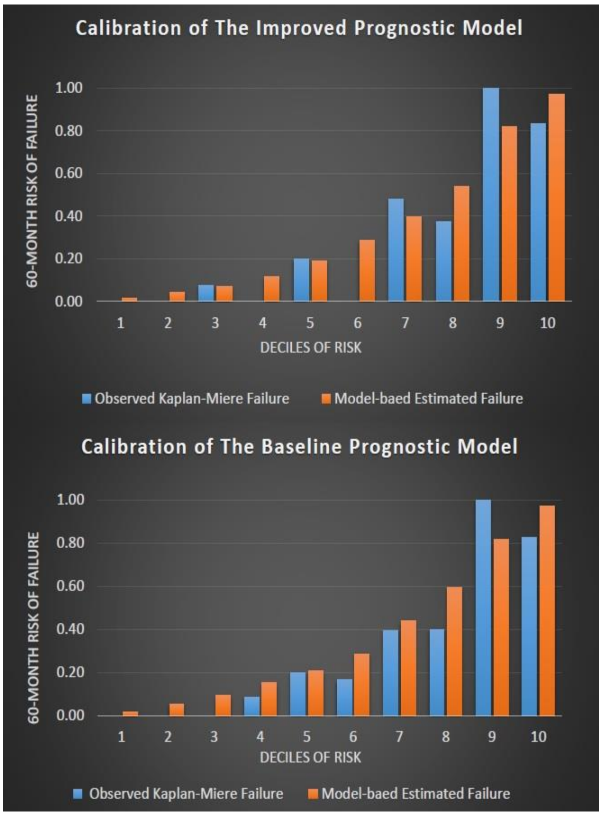

Figure 1. Comparison of calibration of the baseline and improved prognostic model

Table 4. Baseline and improved prognostic model for estimating 60-month risk of all-cause failure after femoral neck fixation with dynamic hip screw

Predictors	HR	95% CI		P	HR	95% CI		P
BMI (kg/m^2)	0.32	0.16	0.64	0.001	0.33	0.17	0.67	0.002
Head-neck trabecular angle (°)	0.49	0.26	0.94	0.031	0.57	0.31	1.02	0.059
High vs low impact energy trauma	3.55	1.08	11.70	0.037	4.45	1.33	14.86	0.015
Varus vs no varus	8.56	2.39	30.57	0.001	8.28	2.27	30.22	0.001
Open vs closed reduction	4.96	1.69	14.59	0.004	5.24	1.79	15.34	0.003
Translation vs no translation	2.65	0.51	13.69	0.245	-	-	-	-

HR: Hazard ratio; BMI: Body mass index

Table 5. Comparing predictive performance of the competing prognostic models

	Baseline prognostic model	Improved prognostic model
Nam-D'Agostino χ^2	7.6, (P = 0.574)	10.1, (P = 0.346)
Harrell's C index,	0.823, 95% CI (0.702-0.953)	0.820, 95% CI (0.680-0.960)
Royston R^2	0.59, 95% CI (0.37-0.73)	0.62, 95% CI (0.43-0.78)
Predictive value added by translation	**Statistics**	**P**
Absolute IDI (95% CI)	0.01 (-0.02- 0.04)	0.668
Relative IDI (95% CI)	0.02 (-0.05- 0.08)	0.660
NRI[1] (95% CI)	0.13 (0.01- 0.24)	0.037
NRI with no cutoff point (95% CI)	0.55 (0.03- 1.08)	0.040

Cutoff points were set at 0.15 and 0.30

CI: Confidence interval; IDI: Integrated discrimination improvement index; NRI: Net reclassification index

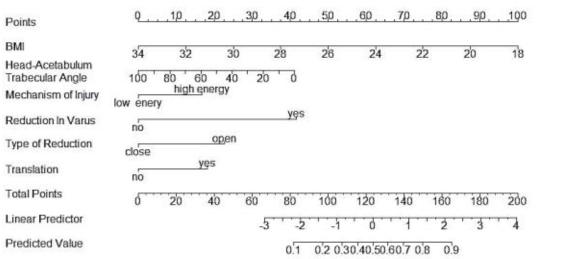

Figure 2. A nomogram developed by incorporating significant predictors modeled without discretizing continuous variables

Other Relevant Findings

Figures 3-8 depict the nonlinearity in the univariate contribution of the candidate continuously-distributed predictors to the 5-year risk of all-cause fracture.

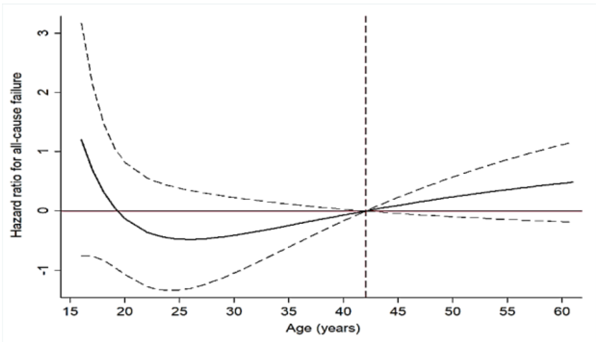

Figure 3. Univariate contribution of the age to the hazard of all-cause failure

Sensitivity Analysis: When we repeated the analysis separately with AVN or fixation nonhealing as the endpoints, with the results remaining essentially the same. As such, to increase the statistical power of the analysis and avoid inflation in the type 1 error, we decided to report the results on non-healing (nonhealing in combination) as the endpoint.

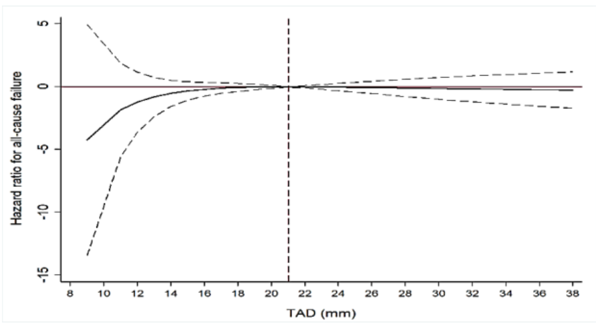

Figure 4. Univariate contribution of the tip-to-apex distance to the hazard of all-cause failure

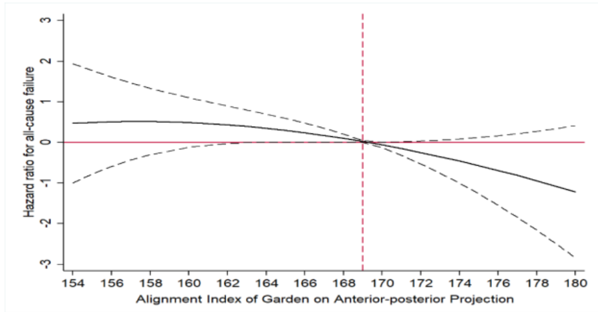

Figure 5. Univariate contribution of the Garden alignment index (GAI) [anterior-posterior (AP) view] to the hazard of all-cause failure

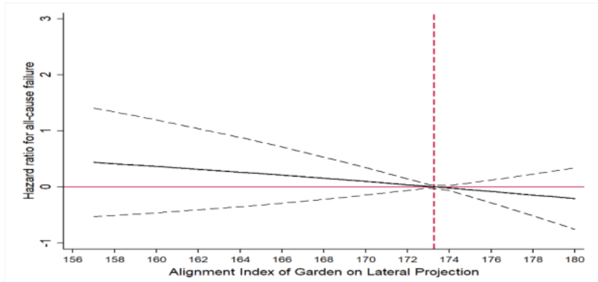

Figure 6. Univariate contribution of the Garden alignment index (GAI) (lateral view) to the hazard of all-cause failure

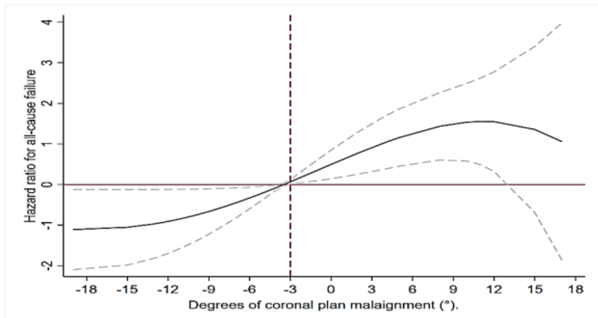

Figure 7. Univariate contribution of the weighted coronal plan maialigment to the hazard of all-cause failure

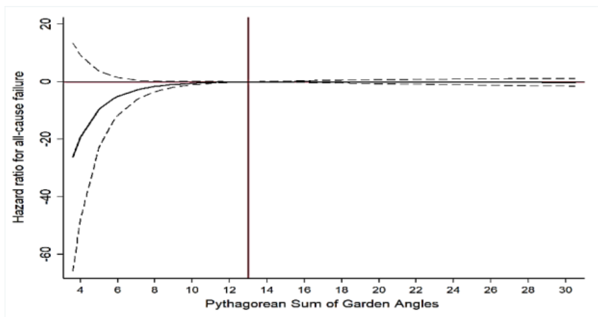

Figure 8. Univariate contribution of the Pythagorean combination of the Garden alignment index (GAI) to the hazard of all-cause failure

Discussion

Studies have reported that the 1-year mortality of hip fractures is around 20-30 percent in the elderly population. In contrast, the survival rate of hip fractures among young adults is > 90% (58). As such, younger patients are more likely to survive long enough to develop complications. Slobogean et al. demonstrated that the incidence of complications experienced by young patients with femoral neck fractures is relatively high. Their findings underscore the further efforts needed to prevent complications in this population. However, with no prediction, there will be no prevention. That is the reason why we attempted to predict development of complications in young adult patients with femoral neck fractures treated by DHS. On a sample contributing to 358 person-year follow-ups, we documented a high rate of uneventful union (59). Using readily available clinical and radiological data, we developed a parsimonious, simple, accurate yardstick to measure the 5-year risk of nonhealing after femoral neck fracture fixation. Utilizing the most recently developed sophisticated statistical methods, we examined the predictive capacity of our prognostic model, which was observed to be a powerful prognostic tool. In order to improve practicality of the prognostication and promote the integration thereof into everyday clinical encounters, we have taken few steps to simplify its application. First, the prognostic model was graphically demonstrated as a nomogram that could be easily used without any advanced knowledge of statistics (available at: https://rpubs.com/mhmmdrz_bzrgmnsh/607332). Second, the nirvana of simplicity is achieved by few clicks on the link: https://drbozorgmanesh.shinyapps.io/DynNomappFNFxPrognostication/. The ease-of-use conferred by theses formats can potentially increase the chance that might be adopted to the clinical practice.

Estimation of the Rate of Nonhealing from Any Causes (All-Cause Nonhealing) after Fixation of Femoral Neck Fractures treated with DHS in Young Adult Patients

On a sample contributing to 358 person-year follow-up, we documented a high rate of uneventful union. Slobogean et al. reviewed 1558 fractures from 41 studies in a meta-analysis. They observed an 18.0% reoperation incidence for isolated femoral neck fractures. The incidence of AVN was reported to be 14.3%, and the corresponding figure for nonunion, malunion, implant nonhealing, and surgical site infection was observed to be 9.3%, 7.1%, 9.7%, and 5.1%, respectively (59).

Identification of the Fracture-, Patient-, or Treatment - Related Factors that Might Have Contributed to the Risk of All-Cause Nonhealing among Potential Predictors, e.g. BMI, High Impact Energy Trauma, or Reduction Techniques

The contribution to the nonhealing of some predictors explored in this study deserves mentioning. The finding that BMI was inversely correlated with the risk of all-cause nonhealing might have been rooted in the fact that BMI can represent the nutritional and consequently bone density status of the patients (60). Numerous studies suggested that TAD is the most important predictive factor for DHS nonhealing, followed by lag screw position, fracture pattern and reduction, patient's age, and presence of osteoporosis (61). TAD contributes to the fixation nonhealing, however, in the current study we used a combination of complications as nonhealing. This approach might have potentially diluted the explanatory effect of TAD. However, the associations remained unchanged in an ancillary sensitivity analysis where the endpoint was defined as fixation nonhealing. Most of the studies reporting on the importance of the TAD have been conducted on elderly populations. In our sample with the mean age of 42 years, TAD might did not play the same role it did among older patients. Besides, high impact energy trauma was found to be a strong predictor of the all-cause nonhealing after femoral neck fracture. Femoral neck fractures are uncommon in young adults and are often the result of high-energy trauma (53). The importance of this finding becomes more evident when it is looked upon in the light of the fact the median age of Iranian population is around 30 years. The major determinant factors for outcomes in the treatment of young adult femoral neck fractures are fracture initial displacement and the quality of reduction. The GAI classes so perfectly predicted the all-cause nonhealing that led to quasi complete separation of data points. One of the most important factors for osteosynthesis is the quality of fracture reduction (58). We observed that fractures fixed in varus position and those not amenable to closed reduction were most likely to be complicated by call-cause nonhealing.

Development and Validation of a Prognostic Model Using Simple Clinical and Readily Available Radiologic Information to Predict the Risk of Nonhealing of Femoral Neck Fractures among Young Adults Treated with DHS

We observed that a model incorporating BMI, HATA, high impact energy trauma, varus reduction, open reduction, and translation (basic parsimonious model) can be used to estimate the 5-year risk of all-cause nonhealing after femoral neck fracture fixation in young adults. Although the hazard ratio for all-cause nonhealing of the translation did not achieve statistical significance, we preferred to retain it in the final prognostic model, because it added to predictive value of the final parsimonious model. This improved prognostic model achieved better predictive power in terms of calibration and discrimination. Both the parsimonious baseline and improved prognostic model predicted 5-year risk of all-cause nonhealing after femoral neck fixation with excellent discriminatory power and were both well-calibrated. The enhanced prognostic model was more complex and parsimonious, however, as compared to the risk classes assigned by the baseline model, it reclassified participants who developed all-cause nonhealing into higher classes of risk and those who did not into lower classes of risk.

Graphical Presentation of the Developed Prognostic Model as a Nomogram that Could Easily be Utilized in Everyday Clinical Encounter and Development of a Web-based Calculator for Estimating the Risk of Nonhealing

In order to improve the practicality of prognostication and promote the integration thereof into everyday clinical encounters, we have taken few steps to simplify its application. First, the prognostic model was graphically demonstrated as a nomogram that could be easily used without any advanced knowledge of statistics (available at: https://rpubs.com/mhmmdrz_bzrgmnsh/607332).

Second, the nirvana of simplicity is achieved by few clicks on the website link: https://drbozorgmanesh.shinyapps.io/DynNomappFNFxPrognostication/. The ease-of-use conferred by these formats can potentially increase the chance that they might be adopted to the clinical practice. Clinical practice guidelines are theoretically thought of as the best available synthesis of research in providing clinical care, yet the degree of adoption remains less than optimal (62). Promoting uptake and use of model and algorithms at the point of care delivery represents a final translation hurdle to move scientific findings into practice. Context of practice and characteristics of the intended users are as important as the models' attributes for promoting its adoption (63). Translational statistics is an attempt to promote the statistical findings communication in a precise and available method to the audience with varying knowledge of statistics. The more complex the statistical models become, the harder it becomes to communicate the information they are intended to provide. Statistical models as an informative graphical description play an important role in translating the bench finding into bedside instructions. Nomograms emblem the idea of visualizing statistical models. A dynamic nomogram is a further advancement in this area toward more simplification of more complex models (23, 24, 64).

Comparison with Other Studies

BMI (5), age (14, 15, 18), sex (8, 14), alcohol use (5, 19), smoking (5, 18), physical activity (5, 18), and the mechanism of fractures (14) have been recorded as risk factors of non-healing of the fixation. However, most of the previous studies have been focused on the prognosis of femoral neck fractures in the elderly patients.

However, in contrast to the older population in who low energy trauma is the most common mechanism of injury, the most common mechanism of the injury in younger patients has been reported to be high-energy trauma (14). Accordingly, it is reasonable to presume that the risk factors of femoral neck fracture in young patients differs from those in their younger counterparts. Some few studies have evaluated the risk factors in young adults, including delayed fixation, alcohol use, smoking, operative time, fracture type, high-energy trauma, renal disease, and respiratory disease (18, 65, 66). Therefore, in the current study we attempted to explore the risk factors of non-healing in a young Middle Eastern population and observed that BMI, HATA, high impact energy trauma, and reduction techniques were independently associated with the risk of no healing of the femoral neck fracture. These risk factors can be used to estimate the 5-year risk of all-cause non-healing after femoral neck fracture fixation in young adult.

Limitations

The strengths of the current study lie in its long-term follow-up and sophisticated statistical methods used to develop the prognostic model. A simple parsimonious prognostic model was developed and demonstrated to accurately estimate the 5-year risk of all-cause nonhealing complicating femoral neck fracture. A multivariate prognostic tool developed herein outperforms any single prognostic parameters. However, in the everyday clinical encounter, multivariate prognostication is easier said than done. Being demonstrated graphically, the prognostication, however, can easily be done using a nomogram. The nomogram format is unique in that it allows varying combinations of the many continuously- or categorically-distributed variables. As such, nomograms could be distinguished from look-up tables or decision trees, where continuously-distributed variables cannot be processed, and where data availability limits the degree of stratification to avoid empty cells or dead-end branches. Developing nomograms is primarily aimed at providing the most accurate prognostication by extracting as much information as possible from data (65). The web-based calculator can help to combine the risk conferred by multiple variables into a single risk by few clicks. These methods can potentially promote multivariate prognostication that might have been otherwise hard to peruse. Our findings, however, need to be interpreted against the backdrop of its limitations. First, the nature of the study was retrospective. Second, the number of non-union and fixation nonhealing was limited. However, any study performed in the era of modern orthopedics contains it as an inherent obligation paucity of fixation nonhealing (21).

As such, there continues to be a deep need to conduct a number of studies with low nonhealing rates and it might not be prudent to wait for a study with high nonhealing rates, which is, of course, very unlikely to be conducted. Third, combining various endpoints in a single outcome variable might have diluted the adverse effect of some potential predictor which have already been shown to be strongly associated with some but not other endpoints. Having shown that this might have not been the case in the current study, the sensitivity analysis turned our attention to the age difference between studies. We hypothesize that age might have modified the effect on nonhealing of the predictors. A sample of combined old and young patients will be needed to examine this hypothesis. Due to its retrospective nature, this study was not intended [nor was it inherently able] to examine the causality of the potential predictors for nonhealing. As such, instead of overindulging in the statistical significance or clinical relevance of every single potential predictor, we focused on developing a model with acceptable predictive characteristics namely discriminatory predictive power, goodness-of-fit (GOF), and calibration. For example, in-depth investigation of the effect on nonhealing of the open reduction independent of fracture severity might merit further investigation. It must be noted, however, that, although open reduction is more likely in patients with more severe fractures, the severity of the fracture alone might not represent all complex information conferred by open reduction. Open reduction imposes larger incisions and dissection and soft tissue trauma, higher volumes of bleedings, more periosteal damage, longer operation time period, higher rate of infection, etc. that might have not been reflected by the severity of fracture. On the other hand, open reduction might lead to a more anatomic reduction that can reduce the risk of nonhealing. As such, we feel that the effect of open reduction is complicated and a huge sample size might be required to capture the effect of each interacting factor related to open reduction independent of the others. Finally, although the web-based dynamic nomogram makes the risk-estimate "only-few-clicks-away," future studies will be needed to examine the extent to which it can practically promote multivariate prognostication in the everyday clinical encounter.

Conclusion

On a sample of young adults contributing to a 358 person-year follow-up, we documented a high rate of uneventful union. Using readily available clinical and radiological data, we developed a parsimonious, simple, accurate yardstick to measure the 5-year risk of nonhealing after femoral neck fractures among young adults. Utilizing the most recently developed sophisticated statistical methods, we examined the predictive power of our prognostic model, which was observed to be a powerful prognostic tool. In order to add to the ease-of-use and to promote its integration into clinical practice, the prognostic model is demonstrated visually as a statistic nomogram. Dynamic nomogram has also been developed to add to the practicality of the prognostication. Although the web-based dynamic nomogram makes the risk-estimate "only-few-clicks-away," future studies will be needed to examine the extent to which it can practically promote multivariate prognostication in the everyday clinical encounter.

Conflict of Interest

The authors declare no conflict of interest in this study.

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