MEDICAL SCIENCE MONITOR

MEDICAL TECHNOLOGY

e-ISSN 1643-3750
© Med Sci Monit, 2017; 23: 5669-5674
DOI: 10.12659/MSM.904026

Received: 2017.02.24
Accepted: 2017.06.07
Published: 2017.11.28

# Identifying Patients Who Will Most Benefit from Single Photon Emission Computerized Tomography and Computerized Tomography After Femoral Neck Fracture

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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**Source of support:** This work was supported by grants from the National Natural Science Foundation of China (No. 81371966) and the Major Project and Disease of the Shanghai Health System, No. 2014ZYJB0302

**Background:** Single photon emission computerized tomography and computerized tomography (SPECT/CT) is useful for assessing blood supply within the femoral head after femoral neck fracture, but its use in all femoral neck fracture patients is not feasible. Therefore, the present study aimed to identify the patients for whom SPECT/CT examination will be most beneficial.

**Material/Methods:** Sixty-five patients with a unilateral femoral neck fracture who underwent SPECT/CT examination of the hip and were treated via closed reduction and internal fixation with three screws were enrolled between January 2009 and March 2011. A decision tree model (C 5.0) was used to identify the factors that best reflect blood supply and to build a flowchart for identifying patients who would benefit from SPECT/CT.

**Results:** Fracture type was most strongly associated with the Fracture/Normal (F/N) ratio, which reflects the blood supply to the fractured femoral head. Age and the time interval from injury to examination were also associated with the F/N ratio. SPECT/CT examination is most beneficial for patients with a displaced fracture, especially if they are over 58 years old and the time interval from injury to examination is less than 10 days.

**Conclusions:** Our results indicate that elderly people with a displaced fracture are most likely to benefit from SPECT/CT examination, which can show the blood supply to the femoral head within a relatively short window of time after the injury.

**MeSH Keywords:** Factor Analysis, Statistical • Femoral Neck Fractures • Femur Head Necrosis • Tomography, Emission-Computed, Single-Photon

**Full-text PDF:** https://www.medscimonit.com/abstract/index/idArt/904026

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## Background

A fracture of the femoral neck is a serious injury, with an annual incidence of approximately 1/1000 persons; it is a major public health issue and economic burden in healthcare [1]. Avascular osteonecrosis of the femoral head (ONFH) is a severe rather common complication that has been reported in 10–30% of patients after femoral neck fracture [2]. ONFH threatens the functional prognosis in young patients and is life-threatening in elderly patients, with a mortality rate of 20–30% in the year following the fracture [3].

Disturbance of the blood supply is generally considered to be the primary cause of ONFH after a femoral fracture [4,5]. However, current treatment approaches do not routinely assess blood flow within the affected femur. Instead, treatment decisions in cases of femoral neck fracture are based mainly on the Garden classification, which describes the morphological condition and cannot accurately reflect the blood supply status. To predict the occurrence of ONFH and determine the appropriate treatment strategy, it is necessary to assess the perfusion of the residual femoral head after fracture of the femoral neck.

We previously reported that single photon emission computerized tomography and computerized tomography (SPECT/CT) accurately show the status of the blood supply [6] by combining functional information from SPECT and morphological information from CT to quantitatively analyze radionuclide uptake in the femoral head [7,8]. However, SPECT/CT is too expensive to be applied as routine screening for all patients. With the goal of saving medical resources and reducing the financial burden on patients, the present study generated a decision tree model to determine which patients with femoral neck fractures can benefit most from SPECT/CT examination.

## Material and Methods

### Patients

This retrospective study enrolled 65 patients with a unilateral femoral neck fracture who underwent SPECT/CT examination of the hip and were treated via closed reduction and internal fixation with 3 screws in our unit between January 2009 and March 2011. Patients with a history of alcohol or steroid abuse were excluded. Informed consent was obtained from each patient, and the study was approved by Ethics Committee of Zhongshan Hospital, Fudan University. All operations were performed by the same surgeon. The patients were followed up for 2 years, and ONFH diagnoses were made based on magnetic resonance imaging (MRI) as the criterion standard imaging modality for this condition.

### SPECT/CT examination and quantitative analysis

The patients received an intravenous injection of 925-1,110 MBq (25–30 mCi) 99mTc-methylene diphosphonate and then underwent SPECT/CT scanning (Precedence; Philips, Milpitas, CA). A detailed description of the scanning procedure was provided in our previous publication [6]. The SPECT/CT data were analyzed by 2 experienced nuclear physicians without prior knowledge of the fracture type. Briefly, the physicians outlined regions of interest (ROIs) of the same size around the fracture site on both sides of the femoral head. Then, SYNTEGRA (Precedence) was used to calculate the radioactive nuclide count within the ROI, and the results are expressed as $\gamma$ photons/cm$^3$. To minimize the errors caused by radionuclide dose and examination time, the $\gamma$ photons/cm$^3$ ratio for the fractural side divided by that for the normal side (the F/N ratio) was used to reflect the blood supply status within the femoral head on the fracture side.

### Statistical analysis

The IBM-SPSS Modeler 17 (SPSS Inc., Chicago, IL, USA) was used for the decision tree (C 5.0) analysis, and SPSS Statistics 19 was used for the other analyses. The decision tree method belongs to a family of nonparametric regression methods based on binary recursive partitioning of data. In this method, the software automatically searches the data for optimal split variables, builds a decision tree structure, and finally classifies all subjects into homogeneous subgroups with respect to the outcome of interest in a flowchart form. We used the *t* test or rank sum test for group comparisons. In addition, receiver operating characteristic (ROC) curves were generated, and specificity, sensitivity, positive predictive value, and negative predictive value were calculated. P values $<0.05$ were considered significant.

## Results

The 65 patients in this study included 31 men and 34 women, with an age range of 19–84 years (median age, 61 years). The basic clinical characteristics of the patients are shown in Table 1. Representative SPECT/CT images are shown in Figure 1. To identify which factor(s) is most closely associated with ONFH, decision tree models (C 5.0) were used. As shown in Table 2, the F/N ratio was one of the most important factors affecting ONFH and reflected the blood supply to the fracture site.

Given that SPECT/CT cannot be applied in routine screening in most hospitals, it is important to determine which patients are likely to benefit most from SPECT/CT. First, a cut-off value for the F/N ratio was determined via ROC curve analysis, and F/N ratios of 0.65 and 0.85 were found to have the best





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**Table 1.** Patient characteristics.

| | Without necrosis (n=52) | With necrosis (n=13) | P value |
|---|---|---|---|
| Age, years, median (range) | 61.5 (29–84) | 60 (19–79) | 0.20 |
| Gender (F/M) | 31/21 | 3/10 | 0.02 |
| Fracture type | | | <0.001 |
| Garden I | 16 | 0 | |
| Garden II | 21 | 2 | |
| Garden III | 9 | 3 | |
| Garden IV | 6 | 8 | |
| Interval to exam, days | 6.3±7.3 | 4.2±5.1 | 0.35 |
| F/N ratio | 1.5±0.8 | 0.5±0.3 | <0.001 |

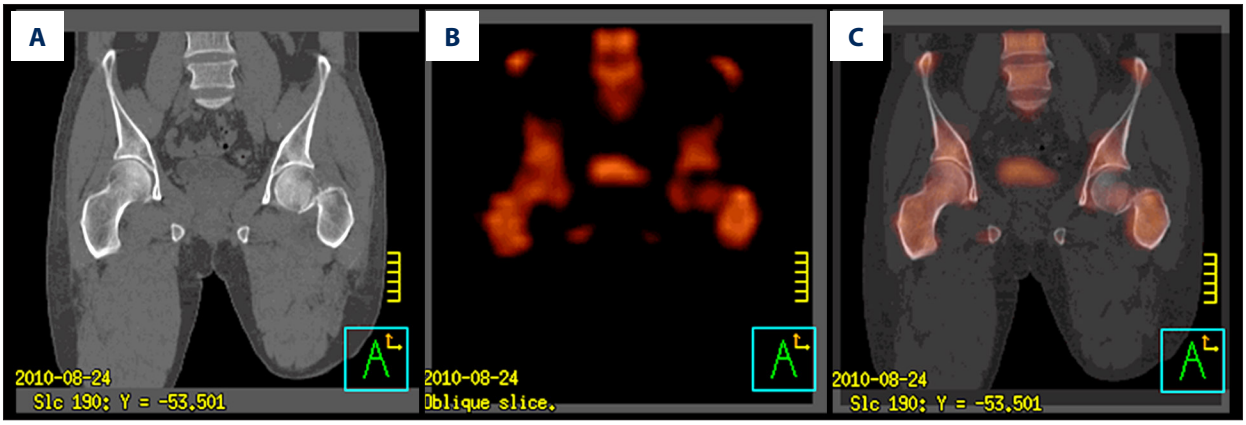


**Figure 1.** SPECT/CT images of a femoral neck fracture. (**A**) CT image; (**B**) SPECT image; (**C**) fused SPECT/CT image.

**Table 2.** Importance of factors for the occurrence of ONFH based on the decision tree C5.0 model.

| Factor | Importance |
|---|---|
| F/N ratio | 0.31 |
| Fracture type | 0.31 |
| Age | 0.12 |
| Gender | 0.12 |
| Interval time | 0.12 |

specificity and sensitivity (Figure 2). From the total group of 65 patients, the decision tree model randomly chose 70% (46 patients) as a training set and 30% (19 patients) as a test set. From the decision tree model, an F/N ratio cut-off of 0.6 was found to be most accurate for identifying patients who should undergo SPECT/CT examination (Table 3).

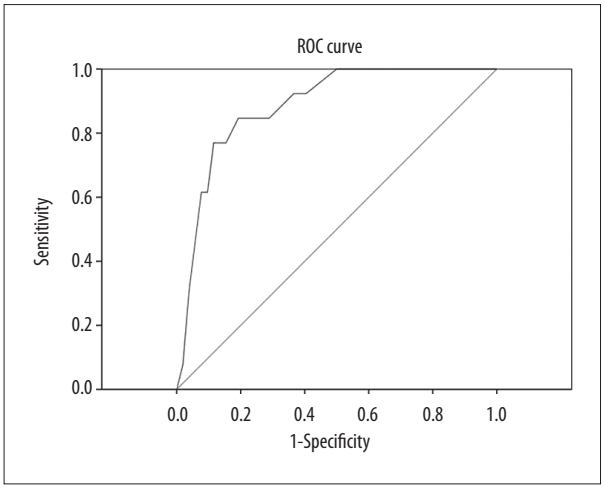


**Figure 2.** Receiver operating characteristic (ROC) curve for the sensitivity and specificity of the F/N ratio determined by SPECT/CT.

Then, the decision tree model (C 5.0) was used to analyze the importance of factors associated with the F/N ratio and to construct a flow chart to help orthopedists decide whether SPECT/CT is indicated for a given patient. As shown in Figure 3, fracture type was most closely associated with the F/N ratio. To a lesser extent, age and the time interval between fracture





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**Table 3.** Validation of decision tree model for patient selection.

| | F/N cut-off 0.6 | | F/N cut-off 0.8 | |
|---|---|---|---|---|
| | Training set | Test set | Training set | Test set |
| Right | 43 | 17 | 41 | 16 |
| Wrong | 3 | 2 | 5 | 3 |
| AUC | 0.928 | 0.969 | 0.881 | 0.871 |
| Gini | 0.855 | 0.938 | 0.762 | 0.743 |

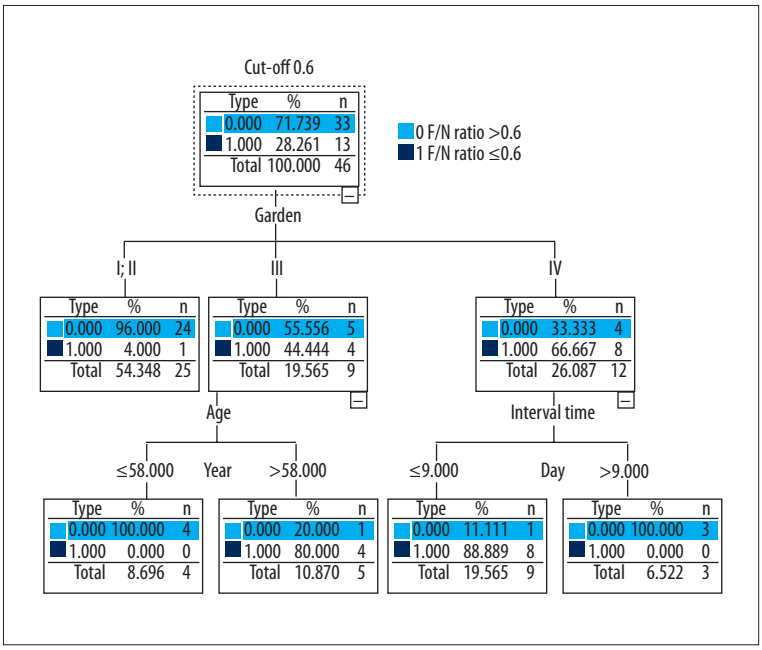


**Figure 3.** Decision tree model for determining whether SPECT/CT is indicated in a patient after femoral neck fracture.

**Table 4.** Validation of decision tree model for predicting ONFH.

| | | Prediction | |
|---|---|---|---|
| | | With necrosis | Without necrosis |
| Actuality | With necrosis | 10 | 3 |
| | Without necrosis | 4 | 48 |

and examination were also associated with the F/N ratio. These results indicated that patients with a displaced fracture who are 58 years or older and those for whom the time interval from injury to examination is less than 10 days are most likely to benefit from SPECT/CT examination to predict impaired blood supply.

The effectiveness of the above model with an F/N cut-off values of 0.6 for predicting the occurrence of ONFH was further validated. Our analysis showed a specificity of 92%, a sensitivity of 77%, a positive predictive value of 71%, and a negative predictive value of 94% for this model (Table 4).

## Discussion

Femoral neck fractures are frequently encountered by orthopedists. An accurate estimation of the risk of avascular necrosis is essential before surgeons and patients make optimized treatment plans. Several factors have been found to be predictive of the development of avascular necrosis, including age, sex, procedure delay, and fracture type [9,10]. There is strong evidence to suggest that the incidence of ONFH is higher among patients with displaced fractures than among those with undisplaced fractures, because displaced fractures are more likely to cause vascular lesions and disrupt the blood supply [11]. This is consistent with our findings that the F/N ratio was one





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of the most important factors related to ONFH and that fracture type was most correlated with the F/N ratio.

Because adequate blood supply is crucial to fracture healing, many studies have attempted to predict femoral head outcomes by directly or indirectly assessing the vascular supply remaining after a fracture [8,12–15]. Although superselective angiography is considered effective in the evaluation of the arteries of the femoral head, it is an invasive procedure and technically difficult for routine and wide use [12]. Dynamic MRI and positive enhancement integral color mapping (PEICM) are non-invasive techniques that use paramagnetic contrast-enhanced signal intensity to compare the vascularity of the femoral head on the fractured side with that of the normal side. These procedures provide an evaluation of femoral head perfusion and demonstrate a high correlation between radiologic and clinical results [16,17]. However, MRI is not indicated for patients with metal implants, such as cardiac pacemakers or cancellous screws, and the use of gadolinium-based contrast agents, however rare, may induce a risk of the nephrogenic systemic fibrosis, a disease involving severe thickening and hardening of the skin overlying the extremities and trunk [18]. SPECT/CT provides another means of checking the blood supply to the femoral head, with 92% specificity and 77% sensitivity, which are comparable to that of MRI. SPECT/CT screening in all patients (not according to specific indications) is impractical and potentially harmful, as SPECT/CT is also expensive and 99mTc is radioactive. Thus, it is important to identify appropriate patients who could benefit most from these examinations. The results of the present study further suggest that elderly patients with a displaced fracture that occurred less than 10 days previously are the best candidates for this examination.

Debates regarding the merits of internal fixation versus arthroplasty for displaced fractures have continued for decades. An international survey conducted in multiple centers showed that internal fixation is the operation of choice for intracapsular displaced hip fractures in patients younger than 60 years, whereas arthroplasty is preferred for patients over 80 years [19]. A meta-analysis comparing internal fixation to arthroplasty for displaced fractures in patients over age 65 years showed a higher revision rate after internal fixation [20]. Our results indicate that patients with an F/N ratio less than 0.6 have a greater risk of ONFH after a displaced fracture, and this cut-off value can be used as a reference value to help orthopedists and patients make informed decisions regarding operative management.

Data mining is a method of analysis in which data are explored to discover hidden patterns and relationships without setting a specific hypothesis [21]. Decision tree analysis, the major form of data mining analysis, was used to screen meaningful factors to build predictive models in our study. To the best of our knowledge, this is the first study to recommend that certain femoral neck fracture patients should undergo SPECT/CT examination based on a decision tree model (C 5.0). Compared to traditional regression models, our decision tree model is simple to interpret by following the flowchart, eliminating the need for specific knowledge of statistics [22].

Limitations of the present study include its retrospective study design and small number of patients. Thus, the conclusions of the study must be further confirmed in a prospective study with a larger sample size.

## Conclusions

Our decision tree model (C 5.0) can be used to decide whether SPECT/CT examination is likely to be beneficial for a patient with a femoral neck fracture. Specifically, SPECT/CT is most needed to assess blood supply in elderly patients with a displaced fracture that occurred less than 10 days previously. Moreover, patients with an F/N ratio less than 0.6 are more likely to develop ONFH.

### Conflicts of interest

None.

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