

The natural history of traumatic femur head necrosis after femoral neck fracture in children and adolescent: a retrospective case series of 64 patients

Fan Yang

Guangzhou University of Chinese Medicine

Yonggang Tu

Dongguan eastern central hospital

Zhinan Hong

Guangzhou University of Chinese Medicine

Fengxiang Pang

Guangzhou University of Chinese Medicine

Wei He

Guangzhou University of Chinese Medicine <https://orcid.org/0000-0002-5323-675X>

Qiushi Wei

Guangzhou University of Chinese Medicine

Ziqi Li (✉ ionsev0214@126.com)

Research article

Keywords: traumatic femur head necrosis, femoral neck fracture, natural history, children, adolescent, case series study

Posted Date: March 17th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-17536/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: The natural history of traumatic femur head necrosis (TFHN) after femoral neck fracture (FNF) in children and adolescent is relatively unknown and has never been specifically characterized. As we speculated, the natural history in such population would be poor and characterized as the high risk of femoral head collapse, hip deformity and degeneration in a short term.

Methods: This retrospective case series enrolled 64 children and adolescent with TFHN who treated with observational treatment from 2000.1 to 2018.1. The primary outcomes, such as the progression of femoral head collapse, hip deformity (Stulberg classification) and hip degeneration (Tönnis grade), and their prognostic factors were analysed.

Results: 42 males and 22 females with a mean age of 13 years (6-16 years), were included. A total of 28 hips (44%) showed unsatisfactory outcome and Twenty-five (39%) hips collapsed progressively during a mean follow-up of 48 months (24-203 months). Finally, 38 hips (59%) experienced hip deformity, 20 of them were class IV/V. 34 hips (53%) generally progressed to osteoarthritis, 14 of them were classified as grades II/III. The location of the lesion and the presence of lateral subluxation were found to be independently related to progression of femoral head collapse; however, the presence of lateral subluxation was the only independent risk factor of severe hip deformity and degeneration.

Conclusion: TFHN in children and adolescent is a rapidly progressing disease with a poor natural history characterized by a high risk of femoral head collapse progression. If the lateral subluxation emerged, collapsed cases showed increasingly tendency towards severe hip deformity and degeneration.

Background

Traumatic femur head necrosis (TFHN) is a debilitating, potentially disabling complication that occurs after femoral neck fracture (FNF) in children and adolescent [1, 2]. As TFHN is the most common complication, a meta-analysis that included 30 studies and 935 immature cases revealed an average incidence of 23.5% [3]. Moreover, to the best of our knowledge, a retrospective study that included 239 hips, as the largest known sample size for paediatric FNF, indicated an incidence of 24.5% for TFHN[4]. However, this condition remains foreign to most orthopaedic surgeons because of the rare incidence of primary injury[5, 6].

Numerous studies have attempted to elucidate the incidence of TFHN and the relevant risk factors, but few have provided additional information such as the characteristics of the natural history or the targeted treatment. Mirrored to the experience of adult FHN, or other childhood osteonecrosis caused by other common aetiologies, hip-preserving operations, such as core decompression[7], free vascularized-fibular grafting[8] and hip osteotomy[9], have been used without confirmed evidence. In the absence of clear guidance, surgeons failed to make timely treatment plan, and observational treatment, such as non-weight bearing exercises[5, 10] or pharmacotherapy[11], were used reluctantly.

As we have observed in clinical practice, TFHN rarely has a promising prognosis in children and adolescent. These patients seemingly present with a strong tendency for femoral head collapse, a crucial pathologic change leading to poor outcomes, and hip deformity that occurs with skeletal maturity, which indicates a high risk of hip degeneration in immature patients[12]. We believe that these indicators, including femoral head collapse, hip deformity and degeneration, are the basis of the natural history of TFHN in children and adolescent but that they have not yet been described in detail.

To the best of our knowledge, the largest sample size to date of 64 patients who underwent observational treatment was used for inclusion in the current study, which aimed to analyse the natural history of TFHN in children and adolescent with a hypothesis that the prognosis in this paediatric population would be poor because of the high risk of femoral head collapse, hip deformity and osteoarthritic change.

Materials And Methods

This study was a retrospective study of a clinical case series and was reported according to the STROBE statement [13]. After the approval of the Ethics Committee, a retrospective case study was conducted based on hospitalized patients with TFHN in children and adolescent in our institute from 2000-1 to 2018-1, according to the following inclusion criteria: (1) participants diagnosed with TFHN [1, 14] as a complication of a previous fracture of the femoral neck; (2) patients with no history of corticosteroid administration or alcohol abuse; (3) Epiphyseal plate of femoral head were not closed completely when the fracture occurred; (4) patients with no other complications from FNF, such as nonunion or infection, or from other diseases, such as dysplasia of the hip joint or rheumatoid arthritis; (5) patients with complete medical records or radiographic data; (6) patients who completed a follow-up period of more than 2 years; and (7) patients who had not received hip-preserving surgery except for reduction or fixation of a FNF.

The extracted data consisted of medical record data and radiographic data. We found the medical records and extracted the following items: (1) age, sex and other personal information; (2) contact information used to for follow-up and completion date; (3) symptoms such as pain, limp and restricted hip function; (4) interval between the fracture of the femoral neck and necrosis; (5) information on the presence of reduction or fixation for the FNF; and (6) the follow-up time.

According to our practical experience, only the cases at severe collapsed stage, and combined with hip subluxation were suggested hip preserved operations; Those with significant hip degeneration already were suggested to hip arthroplasty. Patients at early stage or refusing our suggestion of operations would receive observational treatments, consisted of pain relief, restricted weight bearing, and physical treatment, within the first 2 years after diagnosis of TFHN. We did not use any type of anti-osteoporosis medication because of the unknown complications in children and adolescents. Symptomatic treatments consisted of nonsteroidal anti-inflammatory drugs (NSAIDs) or analgesics, as needed. The clinical and radiographic data were assessed at time of diagnosis and serially every 3 to 4 months within the first 2 years after treatment and every 6 months in the third year and subsequently.

Unsatisfactory outcomes were characterized by the conversion to THA or the presence of a “fair or poor result” according to Ratliff’s clinical criteria[1]. Good was defined as “clinical, no or negligible pain; full or minimal restrictive hip movement; and normal activity or the avoidance of games”. Fair was defined as “clinical or occasional pain; hip movement restriction less than 50%; and normal activity or the avoidance of games”. Poor was defined as “clinical or disabling pain; hip movement restriction more than 50%; and restricted activity.”

Radiographic data were collected, including X-ray, CT and MRI data. According to the classification system of the Japanese Investigation Committee (JIC)[15], all hips were classified into four types. Types A, B and C1 were assigned to groups where the necrotic area did not extend to the acetabular edge (inside coverage). Type C2 was assigned to groups where there was inside coverage of the necrotic area. Then, we analysed whether the location of the necrotic area affected the prognosis. The degree of collapse was also measured according to evaluated by concentric circles on both anteroposterior and lateral radiographs using ImageJ (1.52a, National Institutes of Health, USA), referring to previous literatures[16, 17]. With the increasing progression of femoral head collapse, lateral subluxation was defined when Shenton's line was not continuous.

As the three primary outcomes, the progression of femoral head collapse more than 2 mm, hip deformity and hip degeneration were assessed by concentric circles, the Stulberg classification and the Tönnis grade, respectively. The Stulberg classification[12] was used to describe the shape of the femoral head at skeletal maturity and to predict the long-term outcome at the last follow-up. All the hips in all the patients at the last follow-up demonstrated skeletal maturity. Class I/II hips still maintain a spherical femoral head. Class III hips have an ovoid femoral head, and class IV/V hips demonstrate a flattened femoral head. The degree of osteoarthritis was defined according to the Tönnis grade (grade 0 to 3). Grade 0 indicates the absence of degenerative changes; grade 1 indicates mild joint-space narrowing, mild sclerosis evidenced by widening of the sclerotic zone, and small marginal osteophytes; grade 2 indicates moderate joint-space narrowing, moderate sclerosis of the femoral head or acetabulum, and the presence of small subchondral cysts within the femoral head or acetabulum; and grade 3 indicates severe joint-space narrowing (< 1 mm) or obliteration of the joint space and evidence of large subchondral cysts on the femoral head or acetabulum.

All the radiographic characteristics and outcomes were evaluated independently by two experienced orthopaedic surgeons. If inconsistent results existed, a third surgeon would participate and decide the ultimate result.

Statistical analyses were carried out to analyse which factors, such as age, sex, internal fixation, the interval between FNF and TFHN, symptomatic or asymptomatic disease, the presence of collapse at diagnosis, the location of the lesion and the presence of lateral subluxation, would affect the primary outcomes. Then, adjusted-ORs of the factors would affect severe hip deformity (type IV/V) and degeneration most significantly (grade 2/3) were analysed by binary logistic regression. Cox proportional hazard model was used to identify the adjusted-HRs of predictive factors related to femoral head

collapse progression. With an endpoint of the “progression of femoral head collapse” according to X-ray images, a Kaplan-Meier analysis was performed, and survival curves were created with the log-rank test. A value of $p < 0.05$ was considered to indicate significance. These statistical analyses were performed using SPSS Statistics (version 25; IBM, USA).

Results

A total of 155 children and adolescents (155 hips) were diagnosed with TFHN from 2000-1 to 2018-1. A total of 115 patients had complete medical records or radiographic data. Thirty-five patients were excluded for receiving hip-preserving surgery after diagnosis. In addition, 80 patients were treated conservatively, 64 of whom had been followed for more than 2 years and were finally analysed in our studies (Fig. 1).

These patients included 42 males and 22 females with a mean age of 13.28 years (6–16 years) when they had FNF. In terms of the internal fixation methods used for the fracture, 8 patients were treated without any surgeries. Six patients were treated via fixation with Kirschner wires. A total of 19 and 31 patients underwent fixation surgery with the use of 2 and 3 cannulated screws, respectively. TFHN was diagnosed on average 13.08 months after the fracture. At the time of diagnosis, only 24 patients were symptomatic, while 40 patients were asymptomatic. Of these, 19 patients suffered from varying degrees of hip pain, 17 patients had a limp, and 9 had restricted hip function. The mean follow-up time was 48.38 months (24–203 months).

Regarding the localization of the necrotic area, 13 patients were classified with type A or B hips (less than two-thirds of the weight-bearing portion). Twenty-four patients were classified with type C1 hips (more than two-thirds of the weight-bearing portion but not extending to the acetabular rim), and 27 patients were classified with type C2 hips (extending to the acetabular rim). In light of the anteroposterior X-ray upon diagnosis of TFHN, 33 and 31 hips remained at the non-collapsed and collapsed stages, respectively. Nineteen hips collapsed by less than 2 mm, 6 hips collapsed in a range from 2 to 4 mm, and 6 hips collapsed by more than 4 mm. When patients were diagnosed, 14.1% (9/64) of hips exhibited lateral subluxation on imaging (Shenton's line was discontinuous). Then, 29.7% (19/64) of hips had lateral subluxation after an average of 33.63 months (24 to 69 months).

At the last follow-up, according to Ratliff's clinical criteria, 36, 17 and 11 patients showed good, fair and poor outcomes, respectively, at the recent follow-up. Five patients with poor clinical outcomes underwent conversion to total hip arthroplasty.

Upon TFHN diagnosis, 48.43% (31/64) of hips had collapsed. Throughout the follow-up time, 39.06% (25/64) of hips progressively collapsed by more than 2 mm. A total of 24.24% (8/33) of hips collapsed at the early stage, and 54.84% (17/31) of the hips that collapsed at the collapsed stage demonstrated collapse progression during follow-up. In addition, 70.31% (45/64) of hips ultimately progressed to the collapsed stage. If we defined collapse progression with an endpoint of more than 2 mm at follow-up, the type of symptoms, JIC classification, initial femoral head collapse and lateral subluxation were four

factors that affected the results in univariate analysis (Table 1). Furthermore, multivariate analysis indicated that the JIC classification (adjusted-HR = 6.127 95%CI = 1.80 ~ 20.85) and the presence of lateral subluxation (adjusted-HR = 5.338, 95%CI = 1.60 ~ 17.76) were prognostic factors for the progression of femoral head collapse (Table 2). The Kaplan-Meier curve showed the cumulative percentage of the progression of femoral head collapse and demonstrated a significant relationship between survival time and these prognostic factors (Fig. 2).

Table 1

The characteristics of TFHN and unadjusted analysis of factors related to primary outcomes

Characteristics	N/mean value	P value		
		Collapse Progression [#]	Severe hip deformity [*]	Severe hip degeneration [*]
Male/female	42/22	0.014	0.292	0.452
Age	13.28 Y	0.944	0.787	0.211
Internal fixation of FNF (Non-surgery/ kirschner wire/hollow screw)	8/37/19	0.224	0.085	0.564
Interval between fracture and TFHN diagnosis	13.08 M	0.847	0.735	0.972
Symptomatic/asymptomatic	24/40	0.001	0.001	0.001
femoral head collapse or not at time of TFHN diagnosis	33/31	0.010	0.001	0.186
JIC classification (AB/C1/C2)	13/24/27	∞0.001	∞0.001	0.003
Subluxation/without subluxation	45/19	∞0.001	∞0.001	∞0.001
TFHN = Traumatic femur head necrosis, FNF = Femur neck fracture, JIC = Japanese Investigation Committee, Y = years, M = months, # = Binary logistic regression, * = Cox multivariate regression analysis				

Table 2

Adjusted analysis of prognostic factors related to primary outcomes of TFHN in children and adolescent

Relative factors	P value and OR or HR (95% CI)		
	Collapse progression [#]	Severe hip deformity [*]	Severe hip degeneration [*]
Male/female	P = 0.897 HR = 0.941 (0.377 ~ 2.350)		
Femoral head collapse (no-collapse versus collapse)	P = 0.169 HR = 1.981 (0.748 ~ 5.244)	P = 0.091 OR = 6.525 (0.741 ~ 55.703)	
Symptom (Symptomatic versus asymptomatic)	P = 0.410 HR = 0.648 (0.231 ~ 1.820)	P = 0.847 OR = 0.787 (0.069 ~ 8.955)	P = 0.324 OR = 2.498 (0.405 ~ 15.396)
JIC classification (AB/C1/C2)	P = 0.004 HR = 6.127 (1.800 ~ 20.853)	P = 0.065 OR = 8.764 (0.876 ~ 87.696)	P = 0.542 OR = 1.825 (0.264 ~ 12.617)
Subluxation (Subluxation versus without subluxation)	P = 0.006 HR = 5.338 (1.604 ~ 17.758)	P = 0.012 OR = 25.821 (2.064 ~ 323.066)	P = 0.033 OR = 13.459 (1.235 ~ 146.64)
TFHN = Traumatic femur head necrosis, JIC = Japanese Investigation Committee, [#] = Binary logistic regression, [*] =Cox multivariate regression analysis			

At the latest follow-up time, 59.38% (38/64) of the patients experienced hip deformity, indicating a devastating result for children and adolescents because of their high demand for hip function for their work and daily life. Specifically, 26 (40.6%), 18 (28.1%) and 20 (31.3%) patients were classified as having class I/II, III and IV/V hips, respectively, according to the Stulberg classification. In univariate analysis, the type of symptom, JIC classification, initial femoral head collapse and lateral subluxation were four factors related to severe deformity (Table 1). However, multivariate analysis indicated that lateral subluxation (adjusted-OR = 25.82 95%CI = 2.064 ~ 323.07) was the only indicator of severe hip deformity (Table 2).

In terms of the Tönnis grade, 53.13% (34/64) of hips generally progressed to osteoarthritis. Twenty (27.8%) hips were classified as grade I, and 10 (13.9%) and 4 (5.6%) hips were classified as grades II and III, respectively. In univariate analysis, the type of symptom, JIC classification, initial degree of femoral head collapse and lateral subluxation were four factors that affected the results ($P \leq 0.05$). (Table 1). However, multivariate analysis indicated that lateral subluxation of the hip (adjusted-OR = 13.46, 95%CI = 1.24 ~ 146.64) was the only indicator of severe hip degeneration.

Discussion

A series of studies, first reported by Ratliff and his colleagues in the 1960s, have portrayed TFHN as a severe complication secondary to paediatric FNF[1, 2]. Since then, the unsatisfactory outcomes of this condition have been repeatedly reported by numerous studies; however, the specific natural history of and relevant risk factors for TFHN in children and adolescent remain unknown. This study is the first, to our knowledge, to address these deficiencies through a retrospective study that included 64 conservatively treated cases, which is thought to be the largest currently utilized sample size. The natural history of TFHN in children and adolescent was characterized in detail by femoral head collapse, hip deformity and hip degeneration, which can aid in the treatment planning process. The most important finding in our study is that TFHN in children and adolescent is a rapidly progressing disease with a natural history characterized by a high risk of femoral head collapse and deformity; some cases showed hip degeneration in the short term when lateral subluxation of the hip appeared.

Several limitations still exist. First and foremost, although more than thirty patients treated surgically in our institute, they were inappropriately enrolled as the control group for a variety of indications. Only the cases at severe collapsed stage, and combined with hip subluxation were suggested hip preserved operations; Those with severe hip degeneration already were suggested to hip arthroplasty. Such outcome will be reported in other study. Numeral included cases in current study who had met our surgical indication were suggested surgical treatment, but they refused for personal reasons, which gave us a chance to observe their rapid progression of disease and poor outcome in a short term. Second, although this investigation is the first, to our knowledge, to describe the natural history of TFHN via a case series of children and adolescent treated with conservative or observational treatment, the disease progression and related factors reported in our results were not absolutely equivalent to the “genuine natural history” that was described through the observation that ideally untreated patients rarely exist. Third, we set up a minimum follow-up of 2 years, and finally presented a middle-term result of 4 years on average. To be sure, it was not a long enough period to describe the complete course for most hip problems in paediatric population. However, under the limited follow-up, our results provided a cautionary and useful note of TFHN in children and adolescent, “rapid deterioration and relevant factors”, that would be beneficial for clinical decision. Further prospective multi-centre control trials with more cases or control groups are suggested to confirm the results.

Femur head necrosis in the paediatric population can be induced by both non-traumatic and traumatic aetiologies. The non-traumatic aetiologies include corticosteroid-associated osteonecrosis, Legg-Calve-Perthes disease, sickle cell disease-induced osteonecrosis and Gaucher’s disease[18]. Unlike non-traumatic cases, TFHN are far less common due to the rare incidence of FNF in children and adolescents. Thus, therapists might remain foreign to TFHN because of the lack of guidelines and consensus documents. According to our study, a distinct difference exists in the natural history of cases of TFHN and other non-traumatic cases of osteonecrosis.

The most intuitive characteristic during our observation of TFHN in children and adolescent was the high incidence of femoral head collapse progression, which is generally considered a turning point indicating poor prognosis in the short term [15]. Eight of 33 hips collapsed at the early stage, and 17 of 31 hips that

collapsed at the collapsed stage demonstrated collapse progression during the follow-up. The presence of collapse primarily depended on the lesion size and the location of the necrotic area, as the large involvement of necrotic lesions results in a high risk of femoral head collapse[14, 15]. We believe that patients with TFHN were susceptible to extensive necrosis due to and large damage of blood supply induced by high-energy primary trauma. Ratliff et al demonstrated the highest incidence of TFHN occupying the total head (type I), followed by partial necrosis of the epiphysis (type II) and necrosis between the epiphyseal plate and the fracture line (type III) [1]. A high risk of total head necrosis, ranging from 35.7–80.7%[1, 5, 19–22], has been confirmed repeatedly by studies on the same subject.

The high risk of large lesions and disease progression does not seem to be common in corticosteroid-associated children and adolescents. Kaste et al used MRI to detect 462 cases of corticosteroid-associated osteonecrosis in children and adolescents, and the overall rate of osteonecrosis and the rate of extensive cases involving > 30% were 21.7% and 6.5%, respectively, with a four-year follow-up. Similarly, Karimova et al reported that the proportion of extensive cases involving > 30% and the rate of lateral involvement (Type C) of osteonecrosis in paediatric and young adult patients with leukaemia or lymphoma were 26.3% (30/114 hips) and 31.6% (36/114 hips), respectively. In contrast, 79.7% (51/64) of hips in this study were defined to have lateral involvement (type C). The actual ratio must be higher in our institute because the remaining patients treated surgically all had hips with largely lateral involvement.

Legg-Calve-Perthes disease is also a common aetiology of childhood osteonecrosis, usually with extensive and severe involvement of the epiphysis. Canavese et al described the prognosis of Legg-Calve-Perthes disease in patients under six years old[23]. According to the Catterall classification, 50 hips had mild involvement (grade I/II), and 116 hips had severe involvement (grade III/IV). Similarly, 358 patients with Legg-Calve-Perthes disease (mean age, 5.8 years) were followed for more than five years with radiographic data by Wiig et al, 87.7% (314/358) of whom exhibited severe involvement (grade III/IV)[24].

However, these severely involved patients with Legg-Calve-Perthes disease had a better prognosis than children and adolescent with TFHN. First, TFHN tended to be associated with severe deformity. The percentages of Stulberg class III and IV/V hips in our study were 28.1% (18/64) and 31.3% (20/64) in patients with TFHN after PFNF. The matched data for patients with Legg-Calve-Perthes disease were 22.4% (26/116) and 10.3% (12/116) in the study of Canavese et al and 36.6% (115/314) and 19.2% (60/314) in the study of Wiig et al. Second, during our follow-up of children and adolescent with TFHN, hip degeneration progressed rapidly, with an incidence of 30% in the first years and 50% in total, which was obvious different from patients with Legg-Calve-Perthes disease, who experienced hardly any osteoarthritic changes in the short term until their 40s and 50s[12].

In general, TFHN seemed to be more susceptible to hip deformity and degeneration compared with Legg-Calve-Perthes disease in paediatric population, finally resulting worse prognosis. As we speculated, the weakened abilities of bone repair and remodelling with older age were other potential causes of poor prognosis in patients with TFHN. The average age of the included patients in our study was nearly 13 years old. In this age group, patients with bone necrosis lack satisfactory repair and remodelling

abilities and show completely different natural histories and pathological processes than younger patients[25, 26]. Spontaneous femoral head repair and remodelling into a spherical shape were never observed in our patients at the collapsed stage. Even with the largest sample size of such condition, the sample still did not report the results for all ages of children and adolescents. For instance, we only included small proportion of children younger than 11 years of age (six cases), who would presumably have a better prognosis.

Hip incongruency and instability secondary to irreversible deformity were the major causes of rapid cartilage damage. According to our multivariate analysis, as lateral subluxation of the hip occurred during the follow-up, the risk increased sharply by 26-fold for severe hip deformity and 13-fold for severe hip degeneration (Table 2). In addition, it was difficult to rule out the adverse effect on cartilage of the femoral head, even chondrolysis, due to the presence of primary dramatic injury. Osteoarthritic changes represented the primary cause of arthroplasty in our patients. Our work determined that the natural history of TFHN in children and adolescent was specific and different from corticosteroid-associated osteonecrosis or Perthes disease. However, such a comparison was theoretical and indirect.

As a sign of a “head at risk”, lateral subluxation of the hip was defined as the strongest independent risk factor for primary outcomes in our results. For immature patients, lateral subluxation signifies poor containment and instability of the hip joint. The former is a widely recognized adverse effect of femoral head remodelling, and the latter increasingly exacerbates hip degeneration. Other recognized prognostic factors of progression of femoral head collapse for most types of osteonecrosis of femoral head, such as the initial degree of femoral head collapse[27], JIC classification[15] and symptoms[28], show no apparent relation to severe hip deformity and degeneration. Therefore, these factors did have value for predicting femoral head collapse, but after collapse, not all hip showed further progression to severe hip deformity and degeneration. If the lateral subluxation emerged, cases at collapsed stage showed increasingly tendency towards severe hip deformity and degeneration in the short term (Fig. 3), otherwise they might keep satisfactory hip condition (Fig. 4).

Conclusions

In summary, our recent study first identified the characterization of the prognosis of TFHN in child and adolescent. Over half of our patients had hip involvement with osteoarthritic changes or femoral head deformities. Therefore, we believe that TFHN in children and adolescent is a rapidly progressing disease with a natural history characterized by a high risk of femoral head collapse. For patients who also have hip subluxation, a sign of “head at risk”, severe hip deformity and degeneration will occur and result in poor outcomes in the short term. For such conditions, the ideal treatment should be targeted at decreasing the risk of femoral head collapse and rectifying the poor containment and hip instability induced by lateral subluxation at the same time.

Abbreviations

TFHN
traumatic femur head necrosis
FNF
femoral neck fracture

Declarations

Ethics approval and consent to participate: All data of patients, including the minors, were got from the Medical records and radiographs with the consent of patients or their guardians.

Acknowledgment: The authors thank Pengfei Xin (Guangzhou University of Chinese Medicine, Guangzhou, China) for helpful assistance on the data extraction.

Competing interests: The authors declare that they have no competing interests.

Authors' contributions: FY analyzed the patient data and drafted the manuscript. ZQL designed the study and extracted the data of patients. YGT and ZNH extracted the data. FXP support the method of the study. WH introduced the background of TFHN and proposed the research ideas. QSW recheck the data and statistical method. All authors read and approved the final manuscript.

Funding: The Current study was supported by National Natural Science Foundation of China (No. 81904226 and 81873327) which has no direct intervention on the study process. The reward of researchers, costs of paper works and the like are covered by the foundation above.

Availability of data and materials: The datasets supporting the conclusions of this article are included within the article and its additional files.

References

1. Ratliff AH. Fractures of the neck of the femur in children. *J Bone Joint Surg Br* 1962, 44-B:528-542.
2. Ratliff AH. Avascular necrosis of the head of the femur, after fractures of the femoral neck in children, and Perthes' disease. *Proc R Soc Med* 1962, 55:504-505.
3. Yerosian M, Horneff JG, Baldwin K, Hosalkar HS. Factors affecting the outcome of fractures of the femoral neck in children and adolescents: a systematic review. *Bone Joint J* 2013, 95-B(1):135-142.
4. Wang WT, Li YQ, Guo YM, Li M, Mei HB, Shao JF, Xiong Z, Li J, Canavese F, Chen SY. Risk factors for the development of avascular necrosis after femoral neck fractures in children: a review of 239 cases. *Bone Joint J* 2019, 101-B(9):1160-1167.
5. Canale ST, Bourland WL. Fracture of the neck and intertrochanteric region of the femur in children. *J Bone Joint Surg Am* 1977, 59(4):431-443.
6. Davison BL, Weinstein SL. Hip fractures in children: a long-term follow-up study. *J Pediatr Orthop* 1992, 12(3):355-358.

7. Gao F, Sun W, Guo W, Wang B, Cheng L, Li Z. Combined with Bone Marrow-Derived Cells and rhBMP-2 for Osteonecrosis after Femoral Neck Fractures in Children and Adolescents: A case series. *Sci Rep* 2016, 6:30730.
8. Zhang CQ, Sun Y, Chen SB, Jin DX, Sheng JG, Cheng XG, Xu J, Zeng BF. Free vascularised fibular graft for post-traumatic osteonecrosis of the femoral head in teenage patients. *J Bone Joint Surg Br* 2011, 93(10):1314-1319.
9. Bartonicek J, Vavra J, Bartoska R, Havranek P. Operative treatment of avascular necrosis of the femoral head after proximal femur fractures in adolescents. *Int Orthop* 2012, 36(1):149-157.
10. Maeda S, Kita A, Fujii G, Funayama K, Yamada N, Kokubun S. Avascular necrosis associated with fractures of the femoral neck in children: histological evaluation of core biopsies of the femoral head. *Injury* 2003, 34(4):283-286.
11. Ramachandran M, Ward K, Brown RR, Munns CF, Cowell CT, Little DG. Intravenous bisphosphonate therapy for traumatic osteonecrosis of the femoral head in adolescents. *J Bone Joint Surg Am* 2007, 89(8):1727-1734.
12. Stulberg SD, Cooperman DR, Wallensten R, . The natural history of Legg-Calvé-Perthes disease. *Journal of Bone & Joint Surgery American Volume* 1981, 63(7):1095.
13. Vandembroucke JP, Von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M, Initiative S. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *PLoS medicine* 2007, 4(10):e297.
14. Mont MA, Cherian JJ, Sierra RJ, Jones LC, Lieberman JR. Nontraumatic Osteonecrosis of the Femoral Head: Where Do We Stand Today? A Ten-Year Update. *J Bone Joint Surg Am* 2015, 97(19):1604-1627.
15. Sugano N, Atsumi T, Ohzono K, Kubo T, Hotokebuchi T, Takaoka K. The 2001 revised criteria for diagnosis, classification, and staging of idiopathic osteonecrosis of the femoral head. *J Orthop Sci* 2002, 7(5):601-605.
16. Kubo Y, Motomura G, Ikemura S, Sonoda K, Hatanaka H, Utsunomiya T, Baba S, Nakashima Y. The effect of the anterior boundary of necrotic lesion on the occurrence of collapse in osteonecrosis of the femoral head. *Int Orthop* 2018, 42(7):1449-1455.
17. Nishii T, Sugano N, Ohzono K, Sakai T, Haraguchi K, Yoshikawa HJCORR. Progression and Cessation of Collapse in Osteonecrosis of the Femoral Head. 400:149-157.
18. Kim HKW, Noelle Larson A, Fletcher ND, Winick N, Kim Y-J. Childhood Femoral Head Osteonecrosis. *Clinical Reviews in Bone and Mineral Metabolism* 2011, 9(1):2-12.
19. Stone JD, Hill MK, Pan Z, Novais EN. Open Reduction of Pediatric Femoral Neck Fractures Reduces Osteonecrosis Risk. *Orthopedics* 2015, 38(11):e983-990.
20. Inan U, Kose N, Omeroglu H. Pediatric femur neck fractures: a retrospective analysis of 39 hips. *J Child Orthop* 2009, 3(4):259-264.
21. Forlin E, Guille JT, Kumar SJ, Rhee KJ. Complications associated with fracture of the neck of the femur in children. *J Pediatr Orthop* 1992, 12(4):503-509.

22. Zolczer L, Kazar G, Manninger J, Nagy E. Fractures of the femoral neck in adolescence. *Injury* 1972, 4(1):41-46.
23. Canavese F, Dimeglio A. Perthes' disease: prognosis in children under six years of age. *J Bone Joint Surg Br* 2008, 90(7):940-945.
24. Wiig O, Terjesen T, Svenningsen S. Prognostic factors and outcome of treatment in Perthes' disease: a prospective study of 368 patients with five-year follow-up. *J Bone Joint Surg Br* 2008, 90(10):1364-1371.
25. Joseph B. Natural history of early onset and late-onset Legg-Calve-Perthes disease. *J Pediatr Orthop* 2011, 31(2 Suppl):S152-155.
26. Joseph B, Mulpuri K, Varghese G. Perthes' disease in the adolescent. *J Bone Joint Surg Br* 2001, 83(5):715-720.
27. Mont MA, Ragland PS, Etienne G. Core decompression of the femoral head for osteonecrosis using percutaneous multiple small-diameter drilling. *Clin Orthop Relat Res* 2004(429):131-138.
28. Hatanaka H, Motomura G, Ikemura S, Kubo Y, Utsunomiya T, Baba S, Kawano K, Nakashima Y. Differences in magnetic resonance findings between symptomatic and asymptomatic pre-collapse osteonecrosis of the femoral head. *European journal of radiology* 2019, 112:1-6.

Figures

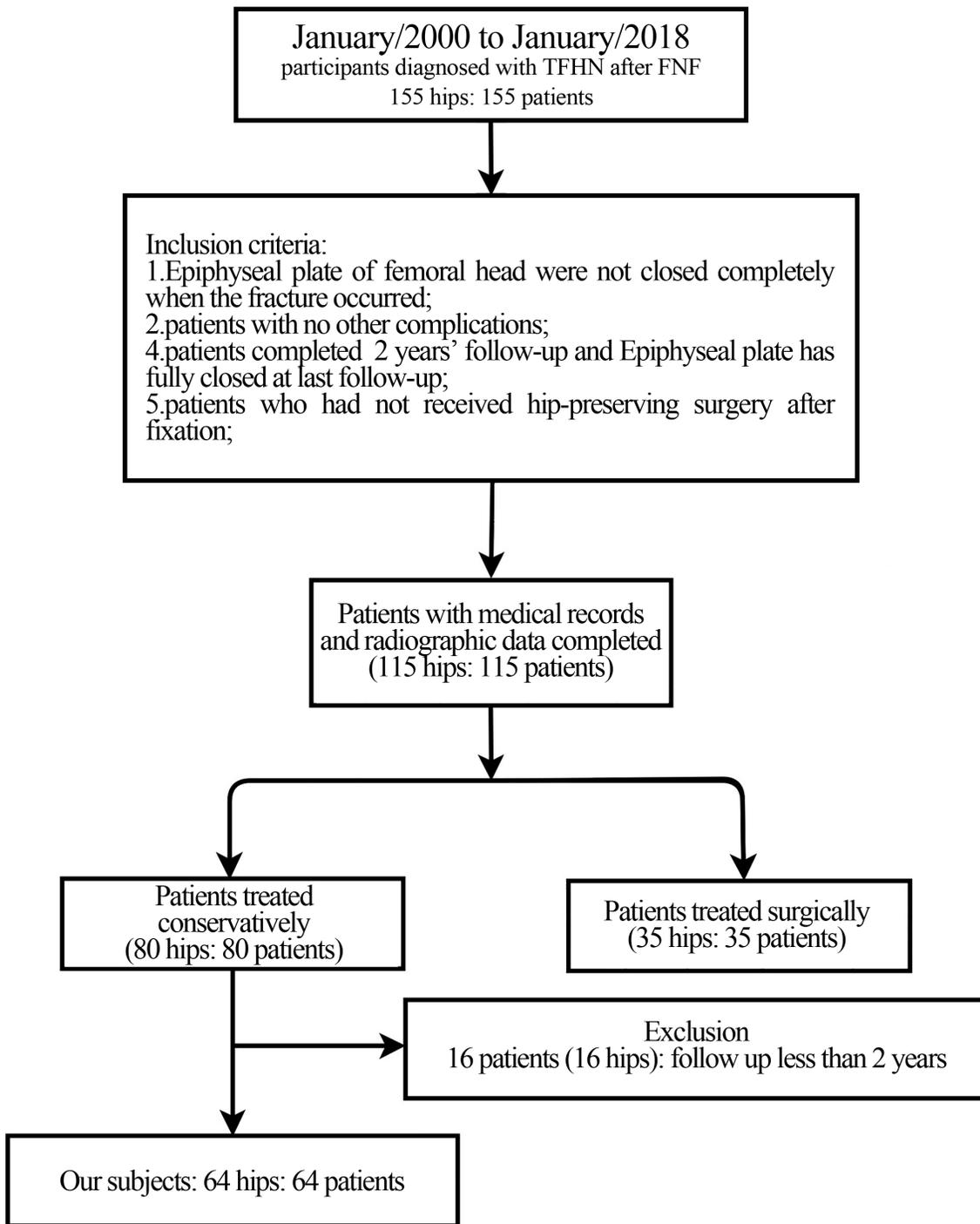


Figure 1

The flow chart of TFHN after FNF in children and adolescent underwent observational treatments.

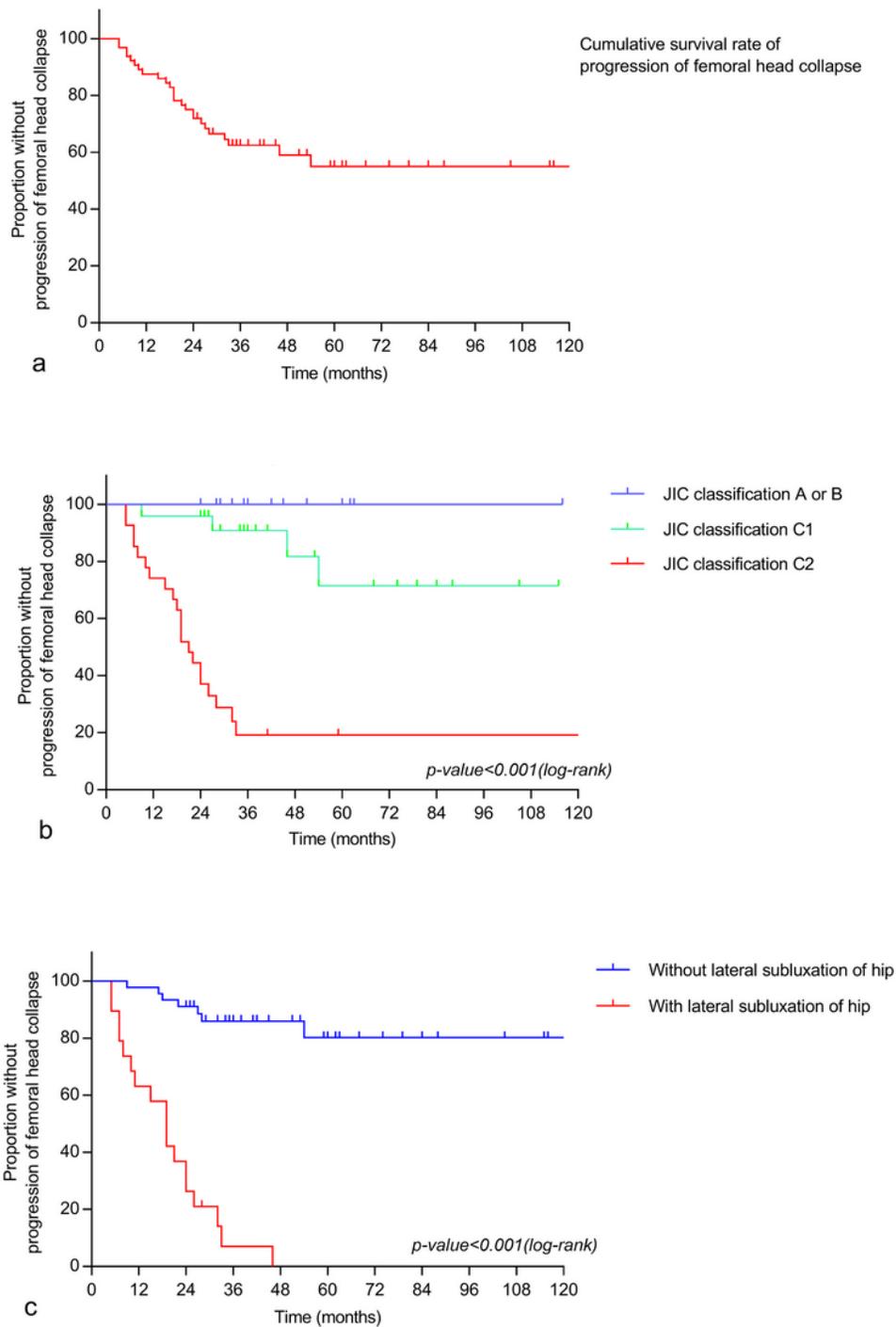


Figure 2

The Kaplan-Meier curve showed the cumulative percentage of the progression of femoral head collapse (a) and demonstrated a significant relationship between survival time and prognostic factors (b, c). With the endpoint of “femoral head collapse progressing more than 2mm”, the overall survival rates were 100.0%, 83.3% and 22.2% in the JIC classification A/B, C1 and C2 respectively (b); the overall survival rates were 15.6% and 94.7% in those without and with lateral subluxation of hip during follow-up.

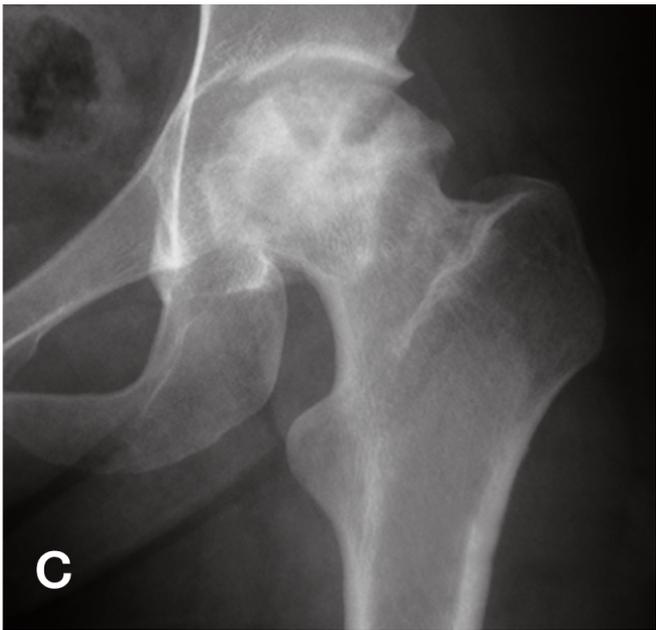
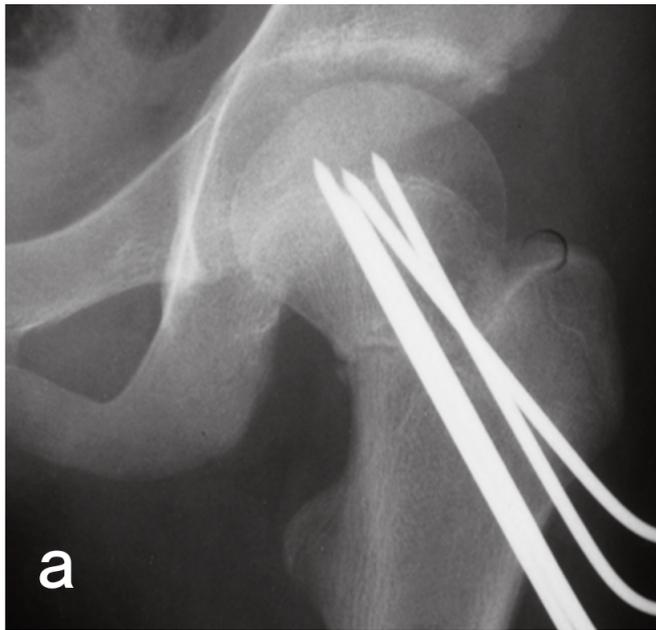


Figure 3

Children of TFHN at collapsed stage showed a satisfactory outcome in a long-term follow-up when their hips were in a stable condition (without lateral subluxation). A female patient of 12 years old, with left FNF, treated with Kirschner wires (a). TFHN (JIC classification C2) was diagnosed three years after FNF (b). During observational treatment, radiographs showed progression of femoral head collapse, but without lateral subluxation (c). At latest follow-up, 16 years after FNF, left hip showed good outcome according to Ratliff's clinical criteria, with moderate hip deformity (Stulberg classification III) and mild hip degeneration (Tönnis grade I).

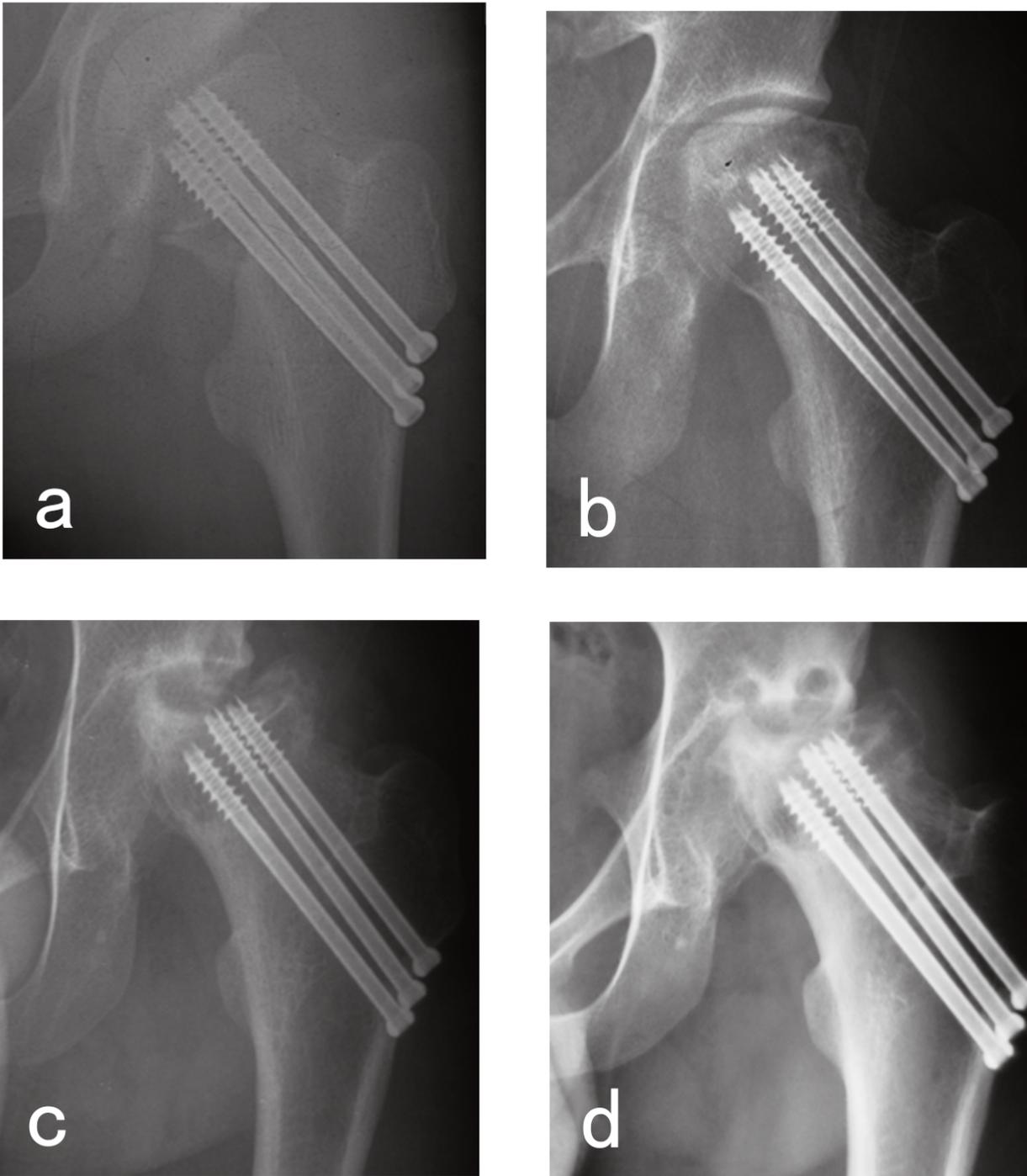


Figure 4

Adolescent of TFHN at collapsed stage showed an increasingly progression towards severe hip deformity and degeneration in the short term, if the lateral subluxation emerged. A male patient of 16 years old, with left FNF, treated with 3 cannulated screws (a). TFHN (JIC classification C2) was diagnosed one year after FNF, which already progressed to collapsed stage with lateral subluxation(b). During observational treatment, radiographs showed progressively femoral head collapse and lateral subluxation 11 months

after diagnosis of avascular necrosis (c). At latest follow-up, 2 years after FNF, left hip showed poor outcome according to Ratliff's clinical criteria, with severe hip deformity (Stulberg classification IV) and hip degeneration (Tönnis grade III).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [additionalfilerevised.xlsx](#)