Clinical outcomes of arthroscopic synovectomy for adolescent or young adult patients with advanced haemophilic arthropathy

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Abstract. The aim of the present study was to assess the clinical outcomes of arthroscopic synovectomy in adolescent or young adult patients with advanced haemophilic arthropathy. From January 2009-January 2012, clinical data from 11 adolescent or young adult patients with advanced haemophilic arthropathy who were treated with arthroscopic synovectomy were retrospectively collected. The mean follow-up period was 71.91±5.28 months. The evaluated indicators included frequency of joint bleeding, range of motion (ROM), X-ray staging, hospital for special surgery (HSS) knee score and HSS pain scores. Joint bleeding frequency, pain degree and HSS scores significantly improved following arthroscopic synovectomy at the end of the follow up period. The ROM did not significantly improve. Among the 11 patients, radiographic stage remained unchanged in 9 cases whereas the remaining 2 cases progressed from stage IV to stage V. No patients required total knee arthroplasty through the end of the follow-up period. These findings suggested that arthroscopic synovectomy appears to an effective treatment option to decrease the frequency of bleeding and knee pain, improve knee function and delay knee joint arthroplasty to a certain extent for adolescent or young adult patients with advanced haemophilic knee arthropathy.

Introduction

Haemophilia is a rare hereditary disease. The knee joint is a frequent bleeding site for patients with haemophilia. The most important treatment to prevent knee joint bleeding among patients with haemophilia is coagulation factor replacement therapy (1,2). For patients who do not respond well to conservative treatment and have recurrent bleeding, arthroscopic synovectomy is an important treatment option (3,4). In general, arthroscopic synovectomy is suitable for early haemophilic arthropathy (3,4); however, in underdeveloped regions in developing countries, it remains difficult to ensure early regular continuous coagulation factor replacement therapy for patients with haemophilia (5,6). Instead, the majority of adolescent or young adult patients already have advanced haemophilic arthropathy when they consult an orthopaedic surgeon for the first time (6). For these patients, the most important therapeutic goals are to decrease the frequency of joint bleeding, relieve symptoms and delay knee joint arthroplasty as much as possible.

Arthroscopic synovectomies performed at the Department of Orthopaedic Surgery in The Second Affiliated Hospital of Xi'an Jiaotong University (Xi'an, China) in 11 adolescent or young adult patients with advanced haemophilic arthropathy between January 2009 and January 2012. The present study retrospectively evaluated the clinical outcomes of these cases and attempted to determine whether arthroscopic synovectomy was effective for these patients with advanced haemophilic arthropathy.

Materials and methods

Patients. The present study was approved by the Ethics Committee of the Second Affiliated Hospital of Xi'an Jiaotong University (approval no. 2008067). Written informed consent was obtained from each patient prior to each surgical procedure as wells as for the use of personal information for research purposes. Clinical data was retrospectively collected from adolescent or young adult patients with advanced haemophilic arthropathy who underwent arthroscopic synovectomy between January 2009 and January 2012. A total of 11 patients were included in the present study with a mean age of 18.73±5.55 years. Inclusion criteria were as follows: i) Stage III or IV advanced haemophiliac arthritis; ii) patients who had repeated joint bleeding and chronic pain following conservative treatment; and iii) patients aged 12-34 years. Exclusion criteria were as follows: i) Patients who had haemophilic arthritis at early stages (I and II) or stage V; ii) patients aged <12 or >34 years; and iii) patients who had contradictions for this surgery. In this cohort, all patients were male. All patients were negative for inhibitors. None of the patients

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had concomitant diseases such as hepatitis B, hepatitis C, or other viruses. X-ray staging of haemophilic arthropathy was based on Arnold and Hilgartner's recommendations (7). Stage I did not exhibit skeletal lesions, with only soft tissue swelling. Stage II exhibited osteoporosis and overgrowth of the metaphysis of the joint. The subchondral bone was intact, and the joint space was not invaded. Stage III exhibited subchondral bone cyst formation, with a mild narrowing of joint space. Stage IV exhibited more serious lesions, with a disordered structure of subchondral bone, and a severely narrowed joint space. Stage V had lost the joint space, and the articular surface was severely damaged.

Surgical indications included: i) Repeated joint bleeding that had no response following 3-6 months of conservative treatment, including coagulation factor supplementation, physical therapy, and rehabilitation; and ii) chronic pain caused by haemophilic arthropathy which had no response to conservative treatment.

Surgical contraindications included: Knee joint infection, apparent axial malalignment (up to 5˚ varus or valgus) (8), patellar subluxation, flexion deformity >30˚, active knee flexion <90˚ or severe knee joint adhesions, particularly. when the patella was fixed on the femur.

Preoperative preparation. Prior to surgery, patients underwent examinations of their coagulation factor activity, prothrombin time, activated partial thromboplastin time and inhibitor concentration. At 30 min prior to surgery, coagulation factors were supplemented based on patient body weight so that their activity was at 80-100%. In the first week following the surgery, the concentration of the coagulation factors was maintained at 60-80%. In the second week following the surgery, the concentration of the coagulation factors was maintained at 20-40%. Coagulation factor VIII (Hualan Biological Engineering, Inc., Xinxiang, China) was intravenously injected 2-3 times daily, and coagulation factor IX (Hualan Biological Engineering, Inc.) was intravenously injected 1-2 times daily according to the Expert Consensus in Perioperative Management in Haemophilia Patients Undergoing Orthopaedic Surgery in China (9). The perioperatively administered volumes of coagulation factor VIII or IX for each patient are summarised in Table I.

Surgical procedures. The surgery was performed under general anaesthesia via six arthroscopic approaches: Anterolateral, anteromedial, lateral suprapatellar, medial suprapatellar, posterolateral and posteromedial portal (10). A complete total synovectomy was performed. In particular, it is important to emphasise that the synovium of the posterior compartment had to be resected. The surgery technique is the same as that for routine total arthroscopic synovectomy. When necessary, meniscus resection, articular cartilage debridement and adhesion release could be simultaneously performed. For all 11 patients, extensive synovial hyperplasia accompanied with the deposition of iron-containing hemosiderin was visible via arthroscopy, and the synovial hyperplasia even exhibited a nodular shape (Fig. 1). The suprapatellar bursa of 3 patients expanded abnormally to 2-3 times the normal volume due to repeated bleeding in the joint cavity. In all patients, extensive articular cartilage softening or even articular cartilage full-thickness defects and subchondral bone exposure were visible. In 2 cases, iron-containing hemosiderin deposition was observed on the surface of the damaged articular cartilage (Fig. 1). In 1 case, the articular cartilage exhibited a brown colour and a brittle texture, appearing similar to sugar cubes (Fig. 2). Obvious adhesions in the joint cavity were not detected in any case. Prior to the wound closure, a radiofrequency device was used to vaporise the bleeding sites. A negative pressure drainage tube was placed for 24-48 h. The knee was covered with ice and a bulky compression dressing was applied.

Postoperative treatment. On the first postoperative day, the patient began active knee joint exercise. If pain prevented active movement, continuous passive motion machine functional exercise was completed. Within 1 week following surgery, partial weight bearing was permitted. The aim of postoperative rehabilitation exercise was to maintain the range of motion of the knee to prevent stiffness and maintain muscle strength.

Outcome measurements. The evaluated indicators included the frequency of joint bleeding, range of motion (ROM), X-ray staging (11), hospital for special surgery (HSS) knee score and HSS pain scores (12) (Table II). A higher HSS pain score suggested a lower level of pain. Clinical efficacy based on HSS knee score was defined as the following: Excellent=≥85 points; good=70-84 points; fair=60-69 points; or poor=≤59 points.

Statistical analysis. Qualitative data are expressed as numbers or percentages. The normality of the data was assessed using the Kolmogorov-Smirnov test. Normally distributed continuous data were presented as means ± standard deviation and were compared using paired Student's t-test. Non-normally distributed continuous data were presented as the median and interquartile range and were compared using the paired-sample Wilcoxon test. SPSS (version 11.0; SPSS, Inc., Chicago, IL, USA) was used to analyse the data. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. Of these 11 patients, 9 had haemophilia A with a factor VIII level of <1%, and 2 patients had haemophilia B with a factor IX level of <1%. All patients were negative for inhibitors, and none of the patients were carriers of hepatitis B, hepatitis C or other viruses. The X-ray staging of all cases indicated a stage IV joint lesion (joint space narrowed severely) and no patients exhibited apparent malalignment. The mean follow-up time was 71.91 months (range, 60-80 months).

Frequency of joint bleeding and ROM. At the end of the follow-up period, the mean frequency of joint bleeding incidents per month decreased from 4.73 times preoperatively to 1.36 times postoperatively ($P<0.05$; Table II). The ROM did not significantly change (Table II). The mean 2.7˚ of extension prior to surgery did not significantly change by the final follow-up (data not shown). Prior to surgery, the mean flexion was 112.3˚, and the mean flexion was 113.6˚ at the final follow-up (data not shown).

Table I. Patient characteristics.

Patient	Age (years)	Sex	Concomitant disease	Factor deficiency	Follow-up duration (months)	Perioperative administered factor volume (U)	Involved side
1	13	Male	No	IX	70	29,000	L
2	22	Male	No	VIII	60	39,000	R
3	28	Male	No	VIII	80	37,800	L
4	23	Male	No	IX	76	25,400	L
5	12	Male	No	VIII	68	30,700	L
6	13	Male	No	VIII	70	38,000	R
7	16	Male	No	VIII	72	33,200	R
8	26	Male	No	IX	71	40,000	L
9	17	Male	No	VIII	74	32,500	L
10	21	Male	No	VIII	77	39,000	R
11	15	Male	No	VIII	73	34,000	R

R, Right; L, left.

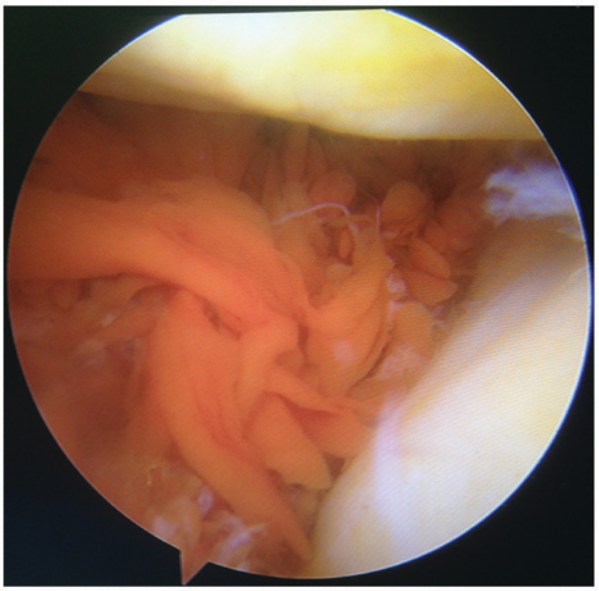

Figure 1. Synovial hyperplasia exhibited a nodular shape and iron-containing haemosiderin deposition was observed on the surface of damaged articular cartilage.

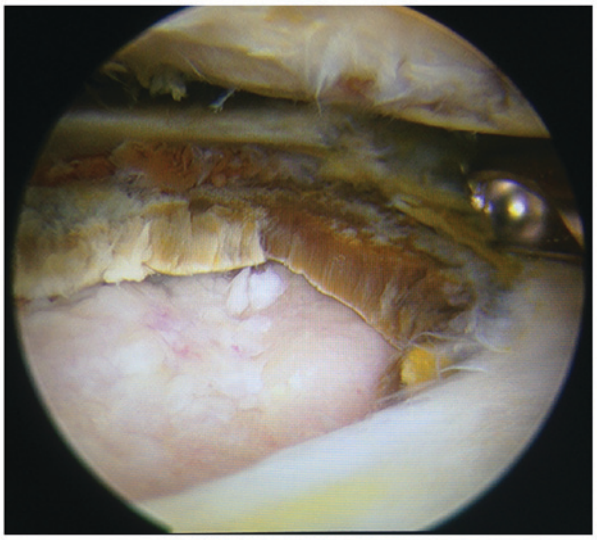

Figure 2. The articular cartilage exhibited a brown colour and a brittle texture, appearing similar to sugar cubes.

Radiographic outcomes. At the final follow-up visit, the radiographic stage remained unchanged in 9 patients, whereas the remaining 2 cases progressed from stage IV to stage V (Table II). No patients required total knee arthroplasty through the end of follow-up. No joint infection, delayed wound healing or non-healing was observed. Preoperative and postoperative radiographs at the final follow up of a representative case are presented in Figs. 3 and 4. The preoperative and postoperative radiographs of this representative case are both stage IV based on Arnold and Hilgartner's recommendations (11) and thus are similar, which suggest a lack of joint lesion progress following surgery.

HSS score. The mean HSS score improved from 50.36 to 71.36 points at the final follow-up ($P<0.05$). The HSS pain scores for the 11 patients significantly increased. The mean pain score prior to treatment improved from 14.09 to 23.18 points at the final follow-up visit ($P<0.05$; Table II).

Complications. In 1 case, joint bleeding occurred in the week following the surgery. Following joint aspiration followed by pressure and bandage application, the symptoms were relieved.

Discussion

Arthroscopic synovectomy is an effective treatment option for repeated joint bleeding that does not respond to conservative treatment (12-16). This technique effectively reduces the frequency of joint bleeding, improves pain, and even increases the range of joint motion (3,8). For patients who are able to undergo arthroscopic synovectomy, it is generally believed that their joint lesions are mild and that the Arnold and

Table II. Effect of arthroscopic synovectomy on ROM, radiographic stage, HSS pain score, HSS knee score and frequency of joint bleeding.

	ROM		Radiographic stage		HSS pain score		HSS knee score		Frequency of joint bleeding	
Patient	Pre	Final	Pre	Final	Pre	Final	Pre	Final	Pre (n/month)	Final (n/month)
1	0/110	0/110	IV	IV	10	30	31	60	5	1
2	0/100	0/100	IV	IV	15	15	44	55	3	0
3	5/95	5/100	IV	IV	10	25	37	70	6	2
4	0/120	0/120	IV	V	20	25	62	80	6	3
5	0/120	0/120	IV	IV	15	30	47	79	4	2
6	0/90	0/100	IV	IV	15	25	50	75	2	0
7	5/110	5/110	IV	V	20	25	66	78	7	1
8	0/150	0/150	IV	IV	20	20	61	68	3	0
9	10/110	20/110	IV	IV	15	25	63	81	5	2
10	0/130	0/130	IV	IV	10	15	58	68	7	3
11	10/100	0/100	IV	IV	5	20	35	71	4	1

ROM is expressed as full extension to full flexion of the knee. ROM, range of motion; HSS, hospital for special surgery.

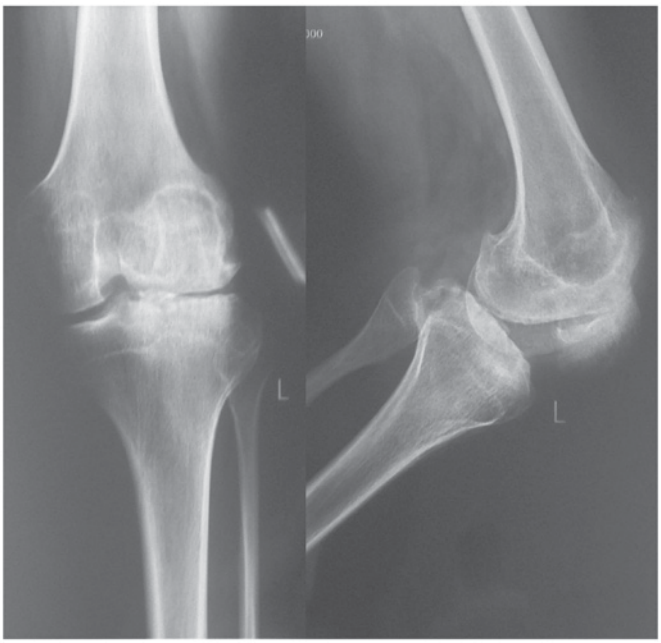

Figure 3. Preoperative X-ray of Patient 3 exhibited a disordered subchondral bone structure and a severely narrowed joint space (stage IV).

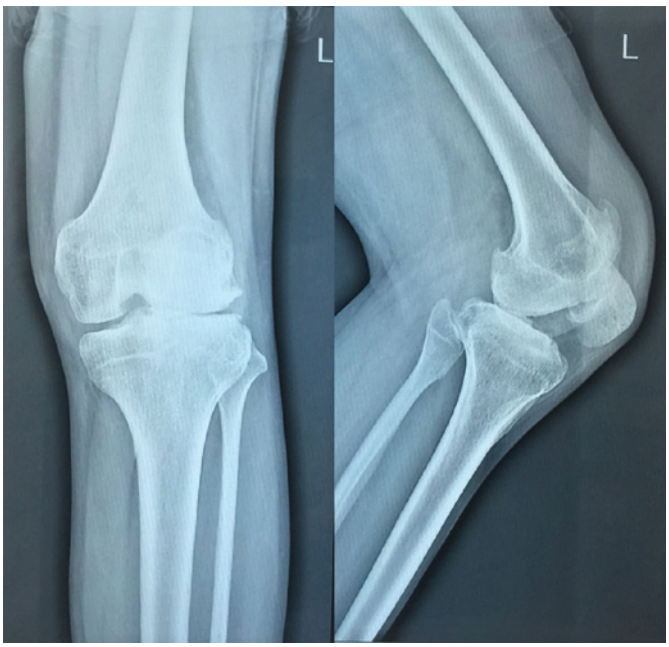

Figure 4. Postoperative X-ray of Patient 3 at the 80-month follow up visit demonstrated no joint lesion progress following surgery (stage IV).

Hilgartner X-ray staging of haemophilic arthropathy should be stage I or II (3,17). In addition, the current consensus is that arthroscopic synovectomy is inappropriate for delaying the progression of joint lesions (3,10,17). However, arthroscopic synovectomy is not the gold standard for haemophilic synovectomy. If radionuclides can be provided, then radiosynovectomy is the first choice for haemophilic synovectomy (8). However, when radiosynovectomy treatment is ineffective or the supply of radionuclide is limited, then arthroscopic synovectomy is a treatment option that should be considered. A previous study has suggested that surgical resection of the synovium should be considered when three consecutive radiosynovectomies have failed (1).

Arthroscopic synovectomy for advanced haemophilic knee joint arthropathy is controversial. In general, its efficacy is considered poor for severe haemophilic arthropathy (8,17). Instead, knee joint arthroplasty is generally recommended (4,10,13). The efficacy of knee joint arthroplasty is certain; in fact, it can greatly improve the quality of life of patients with haemophilic knee arthropathy. For specific patient populations, however, the final selection of the treatment strategy may differ following comprehensively considering all the various factors (9,10).

At present, it is suggested that the only effective method to prevent joint bleeding is to develop a systematic, persistent coagulation factor supplementation programme soon following birth of the haemophilic patient but prior to joint bleeding occurs (3,5,6). Such a programme would be expensive, and on-demand coagulation factor treatment cannot be guaranteed in many parts of the world (5,6). For example, in underdeveloped areas of western China, the prevention and treatment of haemophilia remains far from perfect due to economic, social and other factors (9,10). As many patients do not obtain sufficient early supplementation of coagulation factors, their knee joints have already suffered severe damage during adolescence and young adulthood. The risk of bleeding and infection associated with knee joint arthroplasty for haemophilic arthropathy is greater than the corresponding risk for knee joint arthroplasty among patients with osteoarthritis (18-21). Furthermore, prosthetic survival of knee joint prostheses for haemophilic arthropathy is worse than that of prostheses for osteoarthritis (18-21). Adolescent or young adult patients with advanced haemophilic knee arthropathy may face complications associated with knee joint arthroplasty, necessitating more than one revision arthroplasty in their lifetimes if primary arthroplasty procedures are performed at a younger age (18,20,22). If arthroscopic synovectomy for advanced knee arthropathy can achieve similar improvement in clinical manifestations as that of arthroscopic synovectomy for early arthropathy, then patients may have a few pain-free years with less bleeding, and primary knee arthroplasty can also be delayed for these patients (22,23). For such patients, this procedure would be of great value and worth attempting, particularly for those who are considered to be too young to undergo knee arthroplasty surgery.

A number of studies regarding arthroscopic synovectomy for haemophilic arthropathy have also included some cases of stage IV arthropathy. Yoon *et al* reported 28 cases of arthroscopic synovectomy for haemophilic knee joints (24). Of these cases, the staging of six knee joints was stage IV; however, the clinical results for the stage IV arthropathy were not listed separately. In 1984, Wiedel reported 5 cases of haemophilic arthroscopic synovectomy (including 2 cases of stage IV arthropathy) and suggested that all patients achieved encouraging clinical results (6). For 1 case of stage IV arthropathy, however, the postoperative range of motion did not meet expectations, and manipulation was performed. In 1996, Wiedel reported 9 cases of haemophilic arthroscopic synovectomy, and patients were followed up for 10-15 years (17). These patients included 3 cases of stage IV arthropathy, and 1 case of stage IV arthropathy that progressed to stage V by the end of the follow up period. Of these cases of stage IV arthropathy, 2 did not exhibit postoperative recurrent bleeding events, but 1 case occasionally had recurrent bleeding events. In addition, 1 patient with stage IV arthropathy underwent total knee arthroplasty 8 years following synovectomy. Of the 2 cases of stage IV arthropathy reported by Journeycake (7), the postoperative range of motion of 1 case was improved, whereas that of the other case did not change. At present, no report has clinically studied arthroscopic synovectomy to specifically focus on advanced haemophilic arthropathy, to the best of our knowledge. In the present study, a follow-up evaluation of arthroscopic synovectomies was performed among adolescent or young adult patients with haemophilic advanced knee arthropathy. The present study was notable as it specifically focused on the arthroscopic synovectomy of adolescent or young adult patients with advanced haemophilic knee arthropathy, and the therapeutic significance and value of arthroscopic synovectomy were primarily evaluated for these patients with advanced joint lesions.

The present findings demonstrated that even among patients with advanced haemophilic arthropathy, joint bleeding frequency, pain degree and HSS scores significantly improved following the arthroscopic synovectomy at the end of follow-up, and a significant difference was identified compared with that prior to the surgery. The frequency of joint bleeding was markedly decreased in all cases. However, in case 10, joint bleeding occurred in the week following the surgery. This may be due to surgical trauma and inadequate intraoperative haemostasis. For this case, the symptoms were relieved following joint aspiration followed by pressure and bandage application. All patients exhibited improvement on HSS scores. It was also noted that the pain degree of 2 cases remained unchanged at the final follow-up visit, which is likely associated with advanced joint lesions. The improvement in ROM was not significant, which is likely because preoperative limitations in ROM were not severe, and more aggressive postoperative rehabilitation were not conducted to avoid early postoperative joint bleeding. The results also demonstrated that the radiographic staging of advanced haemophilic arthropathy was not improved following synovectomy and that the staging of 2 cases even progressed, which is consistent with the findings of Wiedel (3,17). However, the deterioration of joint radiographic staging is not necessarily associated with worsening of clinical manifestations; the improvement of clinical manifestation remains beneficial to patients.

X-ray imaging cannot assess changes in joint effusion, or synovitis, nor can X-ray directly identify articular cartilage, which can only be speculated indirectly based on the narrowing of the joint space. Therefore, X-ray examination and scoring are more suitable for haemophilic joints that have existing bone changes (11,25). Magnetic resonance imaging (MRI) is currently recognised as the gold standard for comprehensive radiologic evaluation of joint changes. MRI, especially an MRI scoring system for haemophilic arthropathy, allows us to observe and record the degree of soft tissue involvement and osteochondral involvement (25). However, for patients with severe haemophilic knee arthropathy, it is not necessary to have an overly detailed MRI evaluation, as a detailed scoring difference cannot be associated with differences in treatment strategy or therapeutic effect (25). Therefore, X-ray imaging is suitable for assessing joint involvement among patients with previously described severe haemophilic knee arthropathy with bone changes.

The present study has several limitations. First, as haemophilia is a rare disease, there were a small number of patients recruited. Second, the follow-up period was relatively short. A longer follow-up period is warranted to identify the mean time from arthroscopic synovectomy to knee arthropathy, if knee arthropathy is required.

In conclusion, the present findings suggest that arthroscopic synovectomy is an effective treatment option to decrease the frequency of bleeding and knee pain, improve knee

function and delay knee joint arthroplasty to a certain extent for advanced haemophilic knee arthropathy in adolescent or young adult patients.

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Availability of data and materials

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

Authors' contributions

TZ and XH conceived the study. TZ performed the literature search and writing of the manuscript. SH and SX analysed and interpreted the data. XH submitted the manuscript. HL and FZ collected and assembled the data. All the authors have read and approved the final submitted manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of the Second Affiliated Hospital of Xi'an Jiaotong University (2008067; Xi'an, China). Written informed consent was obtained from each patient prior to the surgical procedures and for the use of personal information for research purposes.

Patient consent for publication

The subjects provided written informed consent for the publication of any associated data and accompanying images.

Competing interests

The authors declare that they have no competing interests

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