Major points

1. Due to the limitation of study design (retrospective study), both selection bias and evaluation bias cannot be avoid. It should be emphasized in the limitation of the study.

Response: Thanks for your constructive comments. In discussion we've revised relevant content in Page 14 & 15 as follows:

Our study had certain limitations. First, limited by the nature of retrospective study design, it must be emphasized that selection bias in patients and evaluation bias are inevitably. Second, our sample size remains small and the duration of follow-up was short. In future research, we should use strict prospective RCT study to verify the findings of our results through longer follow-up.

2. Ethical concern; since this study is retrospective evaluation, how the investigator did inform consent? and how to avoid undue influence from the doctor?

Response: Thanks for your constructive comments. We have revised relevant content and explained the issue concerning ethical concern.

For first question:

Our hospital has a special osteoarthritis (OA) clinic. For patients with initial diagnosis of early osteoarthritis in the out-patient department, they will be recommended for the same senior expert (Dr. Ganke) to carry out the following treatment.

Dr. Ganke will detail the pros and cons of the three treatment options to the patients and emphasize the possible risks, especially the risk of infection in the intra-articular injection, based on the patient's current diagnosis and past medical history. After careful consideration, the patient will select and make a decision of treatment plan, and the patient is informed of the right to change the treatment plan at any time. All patients will sign informed consent and agreed to participate in the study.

For second question:

With regard to avoiding undue influence from the doctor, we take some steps. First, the doctor will avoid expressing personal inclinations during the detailing the treatment options process to reduce patient selection bias. Second, all treatment behaviors are in conflict with the doctor's financial interests. Thirdly, the patient will communicate and be guided by the same doctor to avoid the influence of different doctors' treatment perspectives on patient choice.

We've added relevant content in the method part in Page 7&8.

All patients provided informed consent and agreed to participate in the study. This study was approved by the ethics committee of our hospital.

Ethical committee approval number is 2016NL-036-02

3. Introduction part should contain information regarding pharmacokinetic of IA parecoxib and possible adverse event from IA injection including long term cartilage damage.

Response: Thanks for your constructive comments. We've revised relevant content in introduction as follows in Page 6.

Based on the pharmacokinetics of parecoxib, the half-life of parecoxib in plasma is only 22 minutes because of its rapid conversion to valdecoxib which blocks the synthesis of prostaglandins (PG) in peripheral and central regions, increases the pain threshold, inhibits hypersensitivity of pain threshold, and produces anti-inflammatory and analgesic effects. Parecoxib is conventionally used for postoperative analgesia in the anesthesiology department and surgery department[9-10]. Intra-articular injection of parecoxib can block the inflammatory cascade in early OA by the same mechanism. However, it is undeniable that intra-articular injection has a series of possible adverse events such as injection site inflammation, intra-articular hemorrhage, meniscus or cartilage damage, and even septic arthritis. So this method is rarely discussed in literatures both at home and abroad

4. Statistical analysis: ANOVA should be used instead of t test for multiple comparison and sample size calculation should be calculated.

Response: Thanks for your constructive comments. We've revised relevant content in introduction and explained the issue.

For first question:

Analysis of variance (ANOVA) is also called F-test. In original manuscript we have used AVOVA for multiple comparison and the exact F value has been given. Therefore, we have revised the statement in the text as follows in Page 10.

Continuous numerical variables obeying normal distribution in the three groups were further analyzed by ANOVA

For second question:

Sample size was determined by power analysis using preliminary data obtained in our hospital with the following assumptions: α of 0.05 (two-tailed), power of 90%, difference in HSS Score between three groups of 82 87 94 score in our pilot study, and a standard deviation of 5. Therefore, a minimum of 6 case in each group and 18 cases in total were calculated by Sample size prediction software PASS 11.0. In fact, the sample size of each group in our study is more than 30 cases.

Minor points

1.Title should be changed "the comparison of ..."

Response: Thanks for your constructive comments. The title has revised to the following.

The comparison of intra-articular injection of parecoxib vs oral administration of celecoxib for the clinical efficacy in the treatment of early knee osteoarthritis

2. Abstract: regimen of IA Parecoxib and timing of evaluation should be included.

Response: Thanks for your constructive comments. The method part of abstract has revised as following:

110 patients of early knee osteoarthritis were retrospectively analyzed. These patients were divided into three groups: basic treatment + oral glucosamine (group A, n=37), oral celecoxib + basic treatment + oral glucosamine (group B, n=37), and intra-articular injection of parecoxib + basic treatment + oral glucosamine (group C, n=36) groups. Intra-articular injection of parecoxib was performed once every 2 weeks, at a dose of 40mg each time, for 3 times in total. The three groups were compared in terms of VAS scores, HSS scores and patients' satisfaction before and after treatment. The levels of inflammatory cytokines in the synovial fluid were detected in the three groups before and after treatment.

The result part of abstract has revised as following

All patients were followed up for an average of 15.5±2.7 months. The clinic efficacy was estimated by VAS and HSS scores at 12 months after treatment. Inflammatory cytokine levels in the synovial fluid were evaluated at 3 months after treatment. VAS and HSS scores were significantly improved in each group than before ($P<0.001$). There were significant differences among three groups in VAS and HSS scores ($P<0.001$). The clinical efficacy of group C was superior to that of groups A and B ($P<0.001$), while group B outperformed group A in this respect ($P<0.001$). The patients' satisfaction was the highest in group C ($P<0.001$). After treatment, the levels of TNF-α and IL-6 in the synovial fluid decreased in each group than before ($P<0.001$), while the level of IL-10 increased ($P<0.001$). The three groups differed significantly in the levels of TNF-a, IL-6 and IL-10 in the synovial fluid after treatment ($P<0.001$).

3 Demographic data should include potential confounders; BMI, educational level, marital status, occupation and underlying disease

Response: Thanks for your constructive comments. We've added relevant

content and data as follows in Table 1.

Group	Case	occupation		Marital status		Education Level			underlying disease
		manual worker	mental worker	Married	Single	Primary	Secondary	Higher	HT/DM/ CHD
Group A	37	26	11	35	2	5	25	7	10/3/2
Group B	37	27	10	36	1	4	24	9	11/4/3
Group C	36	25	11	35	1	4	24	8	9/1/1
F/χ^2 value		0.121		0.498		0.41			1.415
P value		0.941		0.779		0.982			0.842

HT: Hypertension; DM: Diabetes mellitus; CHD: Coronary heart disease

4. Reference: Ref number,4,5,6,7,10,12,15,17,18,19 should be rechecked for format and style.

Response: Thanks for your kind suggestion. We have rechecked and revised the Refs format and style