Supplementary material Supplementary material 1 Retrieval strategy. PubMed

#1 ((((Mesenchymal Stromal Cell*[Title/Abstract]) OR (Mesenchymal Stem
Cell*[Title/Abstract])) OR (Mesenchymal Progenitor Cell*[Title/Abstract])) OR (Bone Marrow
Stromal Cell*[Title/Abstract])) OR (Stem cell*[Title/Abstract])
#2 (((((Osteoarthritis[MeSH Terms]) OR (Osteoarthritides[Title/Abstract])) OR
(Osteoarthrosis[Title/Abstract])) OR (Osteoarthroses[Title/Abstract])) OR (knee
osteoarthritis[Title/Abstract])) OR (knee osteoarthrosis[Title/Abstract])) OR
(KOA[Title/Abstract])) OR (knee osteoarthrosis[Title/Abstract])) OR
(KOA[Title/Abstract]))
#3 (((((((platelet-rich plasma[MeSH Terms]) OR (PRP[Title/Abstract])) OR (plasma rich in
growth factors[Title/Abstract])) OR (platelet derived growth factor[Title/Abstract])) OR (platelet

growth factors[Title/Abstract])) OR (platelet derived growth factor[Title/Abstract])) OR (platelet derived[Title/Abstract])) OR (platelet gel[Title/Abstract])) OR (platelet lysate[Title/Abstract])) OR (platelet rich plasma[Title/Abstract]) #4 #1 AND #2 AND #3

EMBASE

#1 'mesenchymal stromal cell*':ab,ti OR 'mesenchymal stem cell*':ab,ti OR 'mesenchymal progenitor cell*':ab,ti OR 'bone marrow stromal cell*':ab,ti

#2 osteoarthritis:ab,ti OR osteoarthritides:ab,ti OR osteoarthrosis:ab,ti OR osteoarthroses:ab,ti OR 'knee osteoarthritis':ab,ti OR 'knee osteoarthrosis':ab,ti OR koa:ab,ti

#3 'platelet-rich plasma':ab,ti OR prp:ab,ti OR 'plasma rich in growth factors':ab,ti OR 'platelet derived growth factor':ab,ti OR 'platelet derived':ab,ti OR 'platelet gel':ab,ti OR 'platelet lysate':ab,ti

#4 #1 AND #2 AND #3

Cochrane Library

#1 (knee osteoarthritis):ti,ab,kw OR (knee osteoarthritides):ti,ab,kw OR (osteoarthritis of Knee):ti,ab,kw OR (Osteoarthritis):ti,ab,kw OR (KOA):ti,ab,kw

#2 (platelet-rich plasma):ti,ab,kw OR (plasma rich in growth factors):ti,ab,kw OR (PRP):ti,ab,kw OR (platelet gel):ti,ab,kw OR (platelet lysate):ti,ab,kw

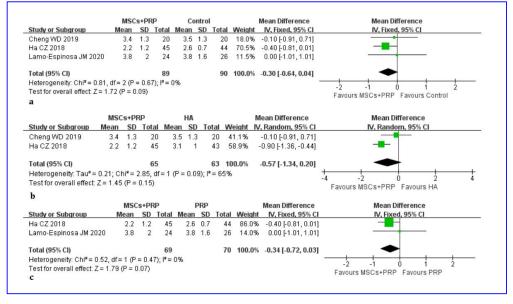
#3 (platelet-rich plasma):ti,ab,kw OR (plasma rich in growth factors):ti,ab,kw OR (PRP):ti,ab,kw OR (platelet gel):ti,ab,kw OR (platelet lysate):ti,ab,kw

#4 #1 AND #2 AND #3

CNKI

(TKA='干细胞') AND (TKA='富血小板血浆' OR TKA='血小板凝胶' OR TKA='血小板') AND (TKA='膝骨关节炎' OR TKA='关节炎' OR TKA='膝关节炎')

Supplementary Figure 1



Supplementary Figure 1 Forest plot of VAS score 3 months after treatment : (a) MSCs+PRP *vs* control group (PRP and HA in control group); (b) MSCs+PRP *vs* HA; (c) MSCs+PRP *vs* PRP.

Supplementary Figure 2

| | MS | SCs+P | Rb. | Co | ntrol | | | Mean Difference | Mean Difference |
|---|---------------------|---------|------------------------|-----------|-------|-------|----------|----------------------|---|
| Study or Subgroup | Mear | n SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% Cl | IV, Fixed, 95% CI |
| Cheng WD 2019 | 3.9 | 3 1.4 | 20 | 4.4 | 1.4 | 20 | 14.0% | -0.50 [-1.37, 0.37] | |
| Ha CZ 2018 | 2.3 | 2 1.1 | 45 | 2.6 | 0.6 | 44 | 78.3% | -0.40 [-0.77, -0.03] | |
| Lamo-Espinosa JM 2020 | 3.3 | 3 2.2 | 24 | 3.5 | 2 | 26 | 7.7% | -0.20 [-1.37, 0.97] | · · · · · · · · · · · · · · · · · · · |
| Total (95% CI) | | | 89 | | | 90 | 100.0% | -0.40 [-0.72, -0.07] | • |
| Heterogeneity: Chi ² = 0.16, | df= 2 (| P = 0.9 | 2); I ² = 0 |)% | | | | | |
| Test for overall effect: Z = 2 | .41 (P= | 0.02) | | | | | | | Favours MSCs+PRP Favours control |
| a | | | | | | | | | |
| | MSCs | PRP | | HA | | | | Mean Difference | Mean Difference |
| Study or Subgroup Me | ean S | D To | tal Me | an SI |) To | tal V | Veight N | V, Random, 95% Cl | IV, Random, 95% Cl |
| Cheng WD 2019 | 3.9 1 | .4 | 20 | 4.4 1.4 | 4 | 20 | 38.6% | -0.50 [-1.37, 0.37] | |
| Ha CZ 2018 | 2.2 1 | .1 | 45 | 3.5 | 1 | 43 | 61.4% | -1.30 [-1.74, -0.86] | |
| Total (95% CI) | | | 65 | | | 63 1 | 00.0% | -0.99 [-1.75, -0.23] | • |
| Heterogeneity: Tau ² = 0.2 | 0: Chi ^z | = 2.60 | df = 1 | (P = 0.1) | 1): P | = 629 | 6 | - | <u> </u> |
| Test for overall effect: Z = | | | | | | | | | -2 -1 0 1 2 Favours MSCs+PRP Favours HA |
| b | | | | | | | | | |
| | M | SCs+P | RP | | PRP | | | Mean Difference | Mean Difference |
| Study or Subgroup | Mea | n SD | Total | Mean | SD | Tota | Weight | IV, Fixed, 95% CI | IV, Fixed, 95% Cl |
| Ha CZ 2018 | 2. | 2 1.1 | 45 | 2.6 | 0.6 | 44 | 91.0% | -0.40 [-0.77, -0.03] | |
| Lamo-Espinosa JM 2020 | 3. | 3 2.2 | 24 | 3.5 | 2 | 28 | 9.0% | -0.20 [-1.37, 0.97] | |
| Total (95% CI) | | | 69 | | | 70 | 100.0% | -0.38 [-0.73, -0.03] | • |
| Heterogeneity: Chi ² = 0.10, | df = 1 | (P = 0. | 75); I= | 0% | | | | | -2 -1 0 1 2 |
| Test for overall effect: Z = 2 | .14 (P = | = 0.03) | | | | | | | -2 -1 U 1 2 Favours MSCs+PRP Favours PRP |
| с | | | | | | | | | Favours MSUS+PRP Favours PRP |

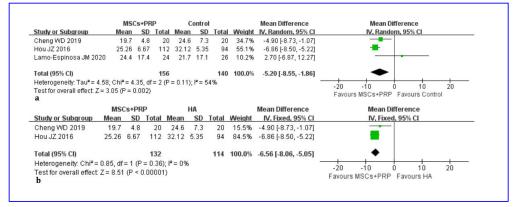
Supplementary Figure 2 Forest plot of VAS score 6 months after treatment : (a) MSCs+PRP *vs* control group (PRP and HA in control group); (b) MSCs+PRP *vs* HA; (c) MSCs+PRP *vs* PRP.

Supplementary Figure 3

| MSCs | +PR | р | | HA | | | Mean Difference | Mean Difference |
|-----------|--|--|---|--|---|--|--|--|
| ean | SD | Total | Mean | SD | Tota | Weigh | t IV, Random, 95% CI | IV, Random, 95% Cl |
| 4.3 | 1.2 | 20 | 4.9 | 1.4 | 20 | 45.0 | 6 -0.60 [-1.41, 0.21] | |
| 2.2 | 1.1 | 45 | 3.9 | 1 | 43 | 55.0 | 6 -1.70 [-2.14, -1.26] | |
| | | 65 | | | 63 | 100.0 | 6 -1.20 [-2.28, -0.13] | - |
| 19; Chi | ² = 5 | .50, df | = 1 (P = | = 0.02 | 2); ² = | 32% | | |
| 2.20 (| (P = (| 0.03) | | | | | | -4 -2 U 2 4 Favours MSCs+PRP Favours HA |
| N. | ASCs | +PRP | | Р | RP | | Mean Difference | Mean Difference |
| Me | an | SD T | otal M | ean | SD T | otal W | ight IV, Fixed, 95% C | I IV, Fixed, 95% CI |
| | 2.2 | 1.1 | 45 | 2.7 | 0.6 | 44 9 | .7% -0.50 [-0.87, -0.13 | g - <mark>-</mark> - |
| | 3.5 | 2.5 | 24 | 4.5 | 2.2 | 26 | .3% -1.00 [-2.31, 0.31 | 1 |
| | | | 69 | | | 70 10 | 0.0% -0.54 [-0.89, -0.18 | 1 🔶 |
| 2, df = 1 | (P= | 0.47); | I ² = 0% | | | | | |
| 2.97 (F | P = 0. | 003) | | | | | | -2 -1 U 1 2 Favours MSCs+PRP Favours PRP |
| | | | | | | | | ravouis Moostrikr ravouis rkr |
| | ean 4.3 2.2 49; Ch 2.20 1 <u>Me</u> 2, df = 1 | lean SD 4.3 1.2 2.2 1.1 49; Chi² = 5 2.20 (P = 0) MSCs Mean 2.2 3.5 2, df = 1 (P = (P = 1) | 4.3 1.2 20 2.2 1.1 45 19; Chi≇ = 5.50, df 2.20 (P = 0.03) MSCs + PRP Mean SD T 2.2 1.1 3.5 2.5 | ean SD Total Mean 4.3 1.2 20 4.9 2.2 1.1 45 3.9 65 65 65 65 49; Chi ² = 5.50, df = 1 (P = 2.20 (P = 0.03) 9 9 MSCs+PRP Mean SD Total M 2.2 1.1 45 3.5 2.5 24 9, df = 1 (P = 0.47); I ² = 0% 69 9 49 46 = 0.47); I ² = 0% 69 | team SD Total Mean SD 4.3 1.2 20 4.9 1.4 2.2 1.1 45 3.9 1 45 5.50, df = 1 (P = 0.02) 0.02 49; Chi ² = 5.50, df = 1 (P = 0.03) 0.03 0.03 MSCs+PRP P Mean SD Total Mean 2.2 1.1 45 2.7 3.5 2.5 24 4.5 9; df = 1 (P = 0.47); P = 0% 69 0.45 0.47 0.45 0.7 | $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | ean SD Total Mean SD Total Weigh 4.3 1.2 20 4.9 1.4 20 45.0% 2.2 1.1 45 3.9 1 43 55.0% 65 63 100.0% 1 43 55.0% 49; Chi ² = 5.50, df = 1 (P = 0.02); P = 82% 2.20 (P = 0.03) 9 1 43 55.0% MSCs+PRP PRP | $\begin{array}{c c c c c c c c c c c c c c c c c c c $ |

Supplementary Figure 3 Forest plot of VAS score 12 months after treatment : (b) MSCs+PRP vs HA; (c) MSCs+PRP vs PRP.

Supplementary Figure 4



Supplementary Figure 4 Forest plot of WOMAC score 3 months after treatment : (a)

MSCs+PRP vs control group (PRP and HA in control group); (b) MSCs+PRP vs HA.

Supplementary Figure 5

| | M | SCs+ | PRP | | Contr | ol | | Mean Difference | Mean Difference |
|---|----------------------|--------------------|-----------|-----------|------------------------|---------|----------------------------------|------------------------|----------------------------------|
| Study or Subgroup | Mea | n S | SD Tot | tal Mea | an S | D Tota | Weight | IV, Random, 95% CI | IV, Random, 95% Cl |
| Cheng WD 2019 | 21 | 4 5 | 5.3 | 20 27 | .8 8. | 3 20 | 35.0% | -6.40 [-10.72, -2.08] | |
| Hou JZ 2016 | 22.4 | 4 5.1 | 19 1 | 12 33. | 34 6.3 | 2 94 | 46.8% | -10.90 [-12.50, -9.30] | • |
| Lamo-Espinosa JM 2020 | 21 | 3 16 | 6.6 | 24 | 23 1 | 5 26 | 18.2% | -1.70 [-10.49, 7.09] | |
| Total (95% CI) | | | 1 | 56 | | 140 | 100.0% | -7.65 [-12.38, -2.92] | • |
| Heterogeneity: Tau ² = 11. | 78; Chi ² | = 7.2 | 9, df = 1 | 2 (P = 0. | .03); I ² : | = 73% | | | -20 -10 0 10 20 |
| Test for overall effect: Z = 3.17 (P = 0.002) | | | | | | | Favours MSCs+PRP Favours Control | | |
| a | | | | | | | | | Favours mods+FRF Favours control |
| | MSCs | +PRF | P | | HA | | | Mean Difference | Mean Difference |
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Cheng WD 2019 | 21.4 | 5.3 | 20 | 27.8 | 8.3 | 20 | 39.7% | -6.40 [-10.72, -2.08] | |
| Hou JZ 2016 | 22.44 | 5.19 | 112 | 33.34 | 6.32 | 94 | 60.3% | -10.90 [-12.50, -9.30] | |
| Total (95% CI) | | | 132 | | | 114 | 100.0% | -9.11 [-13.43, -4.80] | • |
| Heterogeneity: Tau ² = 7 | 37: Chi | ² = 3.6 | 67. df= | = 1 (P = | 0.06): | r = 739 | 6 | | |
| | | | | | | | | | -20 -10 0 10 20 |
| Test for overall effect: Z | | | | | | | | | Favours MSCs+PRP Favours HA |

Supplementary Figure 5 Forest plot of WOMAC score 6 months after treatment : (a)

MSCs+PRP vs control group (PRP and HA in control group); (b) MSCs+PRP vs HA.

Supplementary Figure 6

| | MSC | Control | | | Mean Difference | | Mean Difference | | | | | | |
|--|----------|---------|---------|--------------|-----------------|-------|-----------------|----------------------|--------------|-------------------|------------|-----------------|---------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Fixed, 95% CI | | IV, F | ixed, 95 | % CI | |
| Bastos R 2018 | 68.2 | 24.7 | 9 | 50.3 | 26.6 | 9 | 35.9% | 17.90 [-5.82, 41.62] | | | - | | - |
| Bastos R 2019 | 59.9 | 24.8 | 14 | 54.2 | 24.7 | 16 | 64.1% | 5.70 [-12.05, 23.45] | | - | | | |
| Total (95% CI) | | | 23 | | | 25 | 100.0% | 10.08 [-4.13, 24.30] | | | | | |
| Heterogeneity: Chi2 = | 0.65, df | = 1 (P | = 0.42) | $ ^2 = 0\%$ | 6 | | | - | 1 | 1 | - | + | - |
| Test for overall effect: Z = 1.39 (P = 0.16) | | | | | | | | | -50 Favou | -25 Irs MSCs+P | U RP Fa | 25 vours MSC | 50 s |

Supplementary Figure 6 Forest plot of KOOS 12 months after treatment : MSCs+PRP

vs MSCs.

Supplementary Figure 7

| | MSCs+ | PRP | MSC | S | | Risk Ratio | Risk Ratio |
|-----------------------------------|-----------|-----------|-------------------------|-------|--------|--------------------|-------------------------------|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI |
| Bastos R 2018 | 3 | 9 | 7 | 9 | 69.5% | 0.43 [0.16, 1.15] | |
| Ha CZ 2018 | 3 | 45 | 3 | 43 | 30.5% | 0.96 [0.20, 4.48] | |
| Total (95% CI) | | 54 | | 52 | 100.0% | 0.59 [0.25, 1.36] | - |
| Total events | 6 | | 10 | | | | |
| Heterogeneity: Chi ² = | 0.78, df= | 1 (P = 0) | 0.38); I ² = | 0% | | | 0.05 0.2 1 5 20 |
| Test for overall effect | Z=1.24 (| P = 0.2 | 2) | | | | Favours MSCs+PRP Favours MSCs |

Supplementary Figure 7 Forest plot of adverse reaction : MSCs+PRP vs MSCs.