

## Surgical Approaches in Spontaneous Osteonecrosis of the Knee: Systematic Review

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### A B S T R A C T

**Background:** Spontaneous osteonecrosis of the knee (SONK) is a condition of acute, unilateral knee pain which is caused by destruction of knee's bony structure. Non-surgical treatment could be effective for mild cases. However, surgical treatment should be considered in moderate to severe cases. This systematic review was aimed to determine the outcome of various surgical approaches in SONK patients.

**Methods:** Systematic review was done in accordance to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement. Searching was conducted on PubMed, ScienceDirect, Scopus, ClinicalKey, and Google Scholar. Criteria were set derived from the population of SONK, intervention of surgical methods, and outcome of clinical outcome, including efficacy and safety. Selected studies were appraised using critical appraisal tools by The- Joanna-Briggs Institute for inclusion. Included studies were extracted for characteristics and results, further being analyzed qualitatively.

**Results** Nine studies were found – one discussing each of combination of osteochondral autograft transplantation (OAT) and concomitant high tibial osteotomy (HTO), HTO alone, and total knee arthroplasty (TKA). There were seven studies studying unicompartmental knee arthroplasty (UKA). OAT+HTO provided improvement in Knee Society Score (KSS) knee and function scores alongside 100% survivorship. HTO improved KSS knee and function scores. TKA has no significant complications. UKA was reported to improve KSS symptom, knee, function, patient activity, and patient satisfactory score; Oxford Knee Score (OKS); alongside with low revision and complication rates.

**Conclusions:** Surgical approaches, regardless of the methods, were effective and safe way for treatment of SONK.

## INTRODUCTION

Spontaneous osteonecrosis of the knee (SONK) is a clinical condition of destruction of bony structure of knee which manifested as acute unilateral knee pain accompanied by swelling.<sup>1</sup> It is usually seen in patients aged fifty to sixty years old with active lifestyle.<sup>2</sup> SONK is more common to be found in women with or without history of osteopenia or osteoporosis.<sup>2-4</sup> It is commonly idiopathic and marked with localized osteonecrosis as result of subchondral insufficiency fracture which is observed under the microscope through histopathology examination.<sup>5,6</sup> This fracture is expected to accumulate fluid in the bone marrow which could induce local ischemia and necrosis.<sup>3</sup> Previous systematic review found that there were meniscal tears in 50 to 100 per cent of patients with SONK. Same study also mentioned that SONK severity was correlated with medial meniscus extrusion.<sup>7</sup> Another study suggested that SONK resulted from alteration of posterior medial meniscus root which disrupted knee biomechanics and increased tibiofemoral contact pressures which induced subchondral insufficiency fractures.<sup>3</sup>

SONK patients usually present with acute, unilateral knee pain, and diagnosed either by anteroposterior, oblique, and lateral plain films; or magnetic resonance imaging (MRI) according to

availability.<sup>8</sup> MRI of SONK shows localized edema upon bone marrow of medial femoral condyle which could extend to inter-condylar notch. A additional finding of subchondral crescent could be found on T1- and T2-weighted sequences.<sup>9</sup> SONK is graded into four grades for severity and treatment purposes. Koshino classification has been used to classify SONK, which stage I is defined as clinical complaint alongside with normal radiology findings, stage II is defined as flattening and subchondral radiolucency without collapse on radiology findings, stage III is defined as radiolucency extension with subchondral collapse, stage IV is defined as degenerative changes accompanied by formation of osteophytes and osteosclerosis.<sup>8</sup>

SONK is treated based on the severity and extent of the disease. Non-operative treatment is suitable for early stages of SONK, especially on small (<3.5 cm-square) lesion.<sup>8</sup> Non-operative treatment options including administration of non-steroidal anti-inflammatory medications (NSAIDs), lateral wedge insoles, analgesics, bisphosphonates.<sup>10</sup> Study by Yates mentioned that there were improvements in 20 patients with stage I SONK which were treated by non-operative approach.<sup>11</sup> Surgical techniques used in SONK varies according to the height of the disease. Joint-preserving surgical technique could be applied towards SONK with subchondral collapse. This technique covers a wide range of methods such as arthroscopy, osteochondral autologous transplants, and core decompression. A study by Duany reported that joint preserving surgical techniques had 87% success rate on pre-collapse SONK patients after 40 months of follow up.<sup>12</sup> High tibial osteotomy (HTO), unicompartmental knee arthroplasty (UKA), and total knee arthroplasty (TKA) are preserved for advance stages treatment. HTO is aimed for younger patients with greater physical activity profile. Meanwhile, UKA is known for its ability to maintain native knee kinematics and bone stock.<sup>10</sup> A study reported UKA and TKA effectivity in SONK while surgical indications were applied.<sup>13</sup>

Even though there are varieties of surgical approach for SONK treatment, there is still lack of review covering it. Therefore, this systematic review is aimed to determine efficacy and safety of various surgical approaches for SONK to provide better information for clinicians and researchers on this topic.

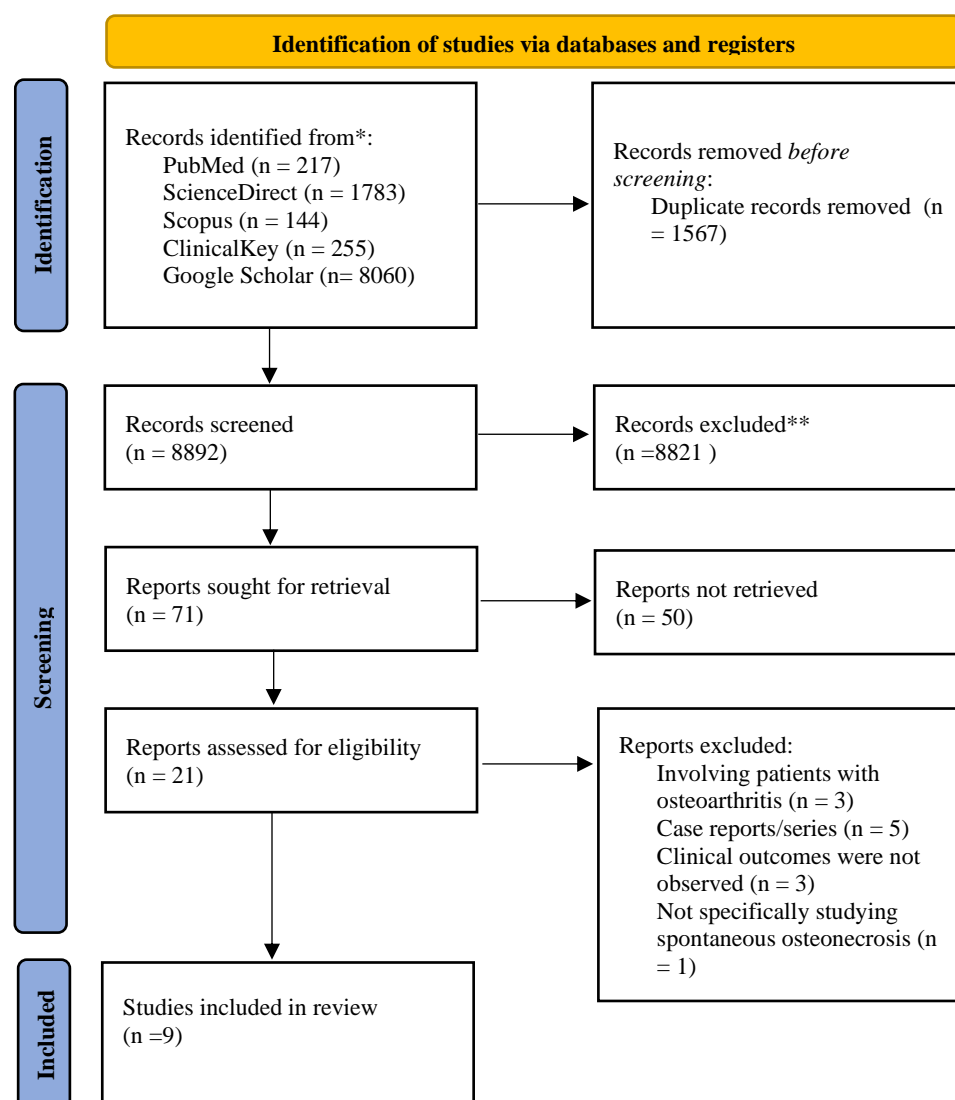
## MATERIAL AND METHODS

A systematic review was conducted with adherence to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guideline.<sup>14</sup> Searching was conducted on PubMed, ScienceDirect, Scopus, ClinicalKey, and Google Scholar using following keywords: "(Osteonecrosis) OR (Osteonecroses) OR (Bone necrosis) AND (Spontaneous) AND (surgery) OR (surgical) OR (operation) AND ((Knee) OR (Genu))". The following inclusion criteria were applied: (1) studying populations of SONK; (2) studying surgical approach as treatment; (3) randomized clinical trial or observational trial; (4) published within the last 10 years. In addition, further studies were excluded: (1) written not in English; (2) no full paper accessible.

Included studies were assessed using critical appraisal tools by The Joanna-Briggs Institute for eligibility towards inclusion.<sup>15</sup> Studies eligible for inclusion were extracted for characteristics (eg. authors, location, age, gender, knee laterality, surgical approach, etc) and results (clinical outcomes: quality of life, recurrence, complications, etc). All data were analyzed qualitatively and presented in results. Studies' data with p value of 0.05 or below were considered statistically significant to be presented.

## RESULTS

Nine cohort studies consisting of five retrospective studies and four prospective studies were assessed after thorough searching and selection (Figure 1). All studies were considered good in terms of the studies' quality after appraisal, hence included in this study (Table 1). A total of 1,152 subjects were collected from nine studies which were conducted across Asia, Europe, and America. Most of the subjects were female, ranging from 44% to 79.2% in each study. All of subjects were adults with minimum and maximum mean age of 66 years old and 74.7 years old, respectively. Most of the subjects were obese with minimum mean of body mass index (BMI) 31 kg/m<sup>2</sup>, which was described Lesion size varies within studies which ranging from 1.2 cm<sup>2</sup> to 5.1 cm<sup>2</sup>. The minimum mean follow up period noted was 2 years with the longest period of 10.3 years (Table 2).<sup>16–24</sup>



**Figure 1.** Searching and selection flowchart of included studies.<sup>14</sup>

**Table 1.** Critical appraisal results of included studies.<sup>15</sup>

Study	Aspect of evaluation											Decision
	1	2	3	4	5	6	7	8	9	10	11	
Kumagai <sup>16</sup>	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Include
Kaneko <sup>17</sup>	Y	Y	Y	UC	UC	Y	Y	Y	Y	NA	Y	Include
Flury <sup>18</sup>	Y	Y	Y	UC	UC	Y	Y	Y	Y	Y	Y	Include
Chalmers <sup>19</sup>	Y	Y	Y	Y	Y	Y	Y	Y	UC	UC	Y	Include
Ma <sup>20</sup>	Y	Y	Y	Y	Y	Y	Y	Y	UC	UC	Y	Include
Kumagai <sup>21</sup>	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Include
Fukuoka <sup>22</sup>	Y	Y	Y	UC	UC	Y	Y	Y	Y	NA	Y	Include
Wu <sup>23</sup>	Y	Y	Y	UC	UC	Y	Y	Y	Y	Y	Y	Include
Pandit <sup>24</sup>	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Include

**Table 2.** Characteristics of included studies.

First author (year)	Design	Surgical method	Location	Sample size	Female (%)	Age (years)	BMI (kg/m <sup>2</sup> )	Lesion size (cm <sup>2</sup> )	Follow up (years)
Kumagai <sup>16</sup> (2022)	RC	OAT + HTO	Japan	43	69.8	67.5 (49-82)	25.4 (18.3-30.8)	5.1 (4.0-8.4)	6.7 (5-10)
Kaneko <sup>17</sup> (2018)	RC	UKA	Japan	61	70.5	74.7 (60-91)	-	-	6.6 (6-10)
Flury <sup>18</sup> (2020)	RC	UKA	Switzerland	37	-	67.5 (54-86)	27.4 (20.8-44)	-	6.9 (2.1-14.2)
	RC	TKA	Switzerland	34	-	66.4 (45-83)	29.5 (20.5-44.7)	-	6.0 (2.0-13.4)
Chalmers <sup>19</sup> (2018)	RC	UKA	United States	45	44	66 (26-91)	31 (19-48)	1.2 (0.6-2.3)	5 (2-12)
Ma <sup>20</sup> (2017)	PC	UKA	China	23	69.6	71.6 (8.14)	25.2 (1.85)	-	5 (2-9)
Kumagai <sup>21</sup> (2022)	PC	HTO	Japan	20	75	69.1 (9.3)	24.5 (5.7)	2.8 (1.4-3.9)	2
Fukuoka <sup>22</sup> (2019)	PC	UKA	Japan	48	79.2	73 (57-83)	24.4	1.7 (1.5-2.2)	8.4 (4-15)
Wu <sup>23</sup> (2021)	RC	UKA	Taiwan	23	74	68.9 (54-80)	26.5 (21.7-33.2)	-	5.6 (5.0-6.3)
Pandit <sup>24</sup> (2015)	PC	UKA	United Kingdom	818	52	66 (32-88)	-	-	10.3 (5.3-16.6)

Abbreviations: RC = retrospective cohort; PC = prospective cohort; OAT = osteochondral autograft transplantation; HTO = high tibial osteotomy; UKA = unicompartmental knee arthroplasty; TKA = total knee arthroplasty; BMI = body mass index

Extraction of studies' results could be seen on Table 3. A total of one study applied osteochondral autograft transplantation (OAT) with concomitant high tibial osteotomy (HTO).<sup>16</sup> Seven studies studying impact of unicompartmental knee arthroplasty (UKA).<sup>17-20,22-24</sup> Meanwhile, there was one study applying HTO and total knee arthroplasty (TKA) each.<sup>18,21</sup> The study which studying impact of OAT and HTO combinations on SONK reported improvement of Knee Society Score (KSS) knee score, function score, alongside with standing femorotibial angle. Same study also reported minimal complications with survival rate of 100%.<sup>16</sup> Study by Kumagai et al which studied impact of HTO on SONK described that there was improvement of KSS knee and function scores, alongside with improvement of mechanical varus into valgus. The same study also reported reduction of interleukin (IL)-6 and -8, and matrix metalloproteinase (MMP) within tissues.<sup>21</sup> One study which applied TKA reported no significant complication observed within populations.<sup>18</sup>

There were three studies on UKA which reported improvement in KSS scores.<sup>17,19,22</sup> A study by Kaneko reported improvement of KSS symptom score, patient activity score, and patient satisfaction score.<sup>17</sup> Improvement of KSS knee score was reported through studies by Chalmers et al and Fukuoka et al.<sup>19,22</sup> Study by Fukuoka et al reported improvement of KSS function score within subjects.<sup>22</sup> Other indicators were also improved. There was one evidence of each improvement of EQ 5-D, range of motion, and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score reported.<sup>17,18</sup> Improvement of WOMAC score was better in UKA populations compared to TKA populations.<sup>18</sup> Oxford Knee Score (OKS) was also reported to be improved in four studies.<sup>20,22-24</sup> Knee flexion was improved in one study.<sup>22</sup>

UKA was subjected to good safety according to various studies. Three studies reported that 10-year survivorship rate ranged from 76 per cent to 90.4 per cent.<sup>17,19,24</sup> Two studies reported minimum revision with one study reported no revision in patients underwent UKA.<sup>17,19,24</sup> Three studies reported no major complication was found and one study reported 2.6% minor complications rate.<sup>18-20</sup>

**Table 3.** Outcomes of included studies.

Study	Intervention	Follow up (years)	Outcomes
Kumagai	OAT+HTO	6.7 (5-10)	Improved mean KSS knee score ( $87.9 \pm 8.6$ vs $48.8 \pm 13.3$ ), function score ( $87.3 \pm 12.2$ vs $60.1 \pm 10.9$ ), standing FTA ( $169.7 \pm 2.4$ vs $181.1 \pm 27.7$ ) ( $p < 0.05$ ) No significant differences in clinical and radiology outcomes in patients aged $\geq 70$ years and $< 70$ years Four cases of lateral hinge fracture around site of osteotomy site and one case of delayed union Survival rate of 100%
Kaneko	UKA	6.6 (6-10)	Improved KSS symptom score ( $21 \pm 5$ vs $11 \pm 6$ ), KSS patient satisfaction ( $31 \pm 8$ vs $17 \pm 9$ ), KSS patient activities ( $79 \pm 19$ vs $52 \pm 14$ ), EQ-5D ( $81 \pm 12$ vs $58 \pm 10$ ), and postoperative range of motions ( $119 \pm 21$ vs $105 \pm 17$ ) ( $p < 0.05$ ) No significant differences of KSS patient expectation score Revision surgery in 1.6% cases due to postoperative fracture of the medial tibial plateau A 90.4% rate of survivorship at 10 years
Flury	UKA v TKA	6.9 (2.1-14.2) and 6.0 (2.0-13.4)	UKA gave better WOMAC score (1.0 vs 1.6, $p = 0.04$ ) compared to TKA No significant KSS pain score difference observed (82 vs 83, $p > 0.05$ ) No significant complication difference observed No correlation between necrotic lesion size and failure rate
Chalmers	UKA	5 (2-12)	Improvement of KSS (94 vs 60) ( $p < 0.05$ ) No surgical complications A 89% five-year survivorship A 76% ten-year survivorship A 93% revision-free rate in five and ten years Conversion into TKA in 6.5% cases No revision done for loosening, fracture, or wear
Ma	UKA	5 (2-9)	Improvement of OKS ( $18.75 \pm 3.76$ vs $39.32 \pm 5.53$ ) ( $p < 0.05$ ) Complication rate of 2.6% including bearing dislocation ( $n = 2$ ), progressive OA ( $n = 1$ ), and superficial infection ( $n = 3$ ) No major complications found
Kumagai	HTO	2	Improvement of KSS knee (MD=33.8) and function (MD=29.4) scores ( $p < 0.05$ ) Change of mechanical varus (-8.6) to valgus (5.2) ( $p < 0.05$ ) Correlations between lesion size and concentrations of IL-6, IL-8, and MMP-13 ( $p < 0.05$ )
Fukuoka	UKA	8.4 (4-15)	No revisions, reoperations, major complications observed Improvement of knee flexion ( $137.5$ vs $128.7$ ), KSS knee score ( $91.3$ vs $52.3$ ), function score ( $90.2$ vs $39.7$ ), and OKS ( $40.2$ vs $21.6$ ) ( $p < 0.05$ )
Wu	UKA	5.6 (5.0-6.3)	Reduced OKS ( $40.65 \pm 4.28$ vs $16.73 \pm 5.06$ ) and VAS scores ( $2.61 \pm 0.72$ vs $8.04 \pm 0.77$ ) ( $p < 0.05$ ) MMPRT in 69.6% patients
Pandit	UKA	10.3 (5.3-16.6)	Mean OKS of 40 (95% CI = 2-48) with 79% knees showed good/excellent outcome 6.7% implant-related reoperations with mean of 5.5 years 10-year survival rate of 94% 15-year survival rate of 91%

Abbreviations: OAT = osteochondral autograft transplantation; HTO = high tibial osteotomy; UKA = unicompartmental knee arthroplasty; TKA = total knee arthroplasty; KSS = Knee Society Scores; FTA = femorotibial angle; EQ-5D = EuroQol 5D; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; OKS = Oxford Knee Score; OA = osteoarthritis; IL = interleukin; MMP = matrix metalloproteinase; MMPRT = MRI-identified medial meniscus posterior root tear; VAS = visual analogue scale



## DISCUSSION

Surgical methods were proven effective and safe for SONK regardless of the methods used. Various studies showed that surgery should be considered when conservative therapy is no longer deemed effective. A study suggested that surgery should be conducted in SONK with grade III or higher.<sup>25</sup> Another studies found that conservative treatment was not effective in SONK with lesion width of more than a half of the condyle.<sup>25,26</sup> Therefore, SONK could give good impact on patients which do not respond towards conservative treatments .

HTO is a procedure which preserve the joint to reduce the load of affected knee compartment in order to improve long-term clinical outcomes.<sup>27,28</sup> It as usually aimed for smaller lesion ( $<4\text{ cm}^2$ ) and could be conjoined with other procedures such as bone marrow stimulation (BMS) or OAT.<sup>29</sup> Several studies reported worse clinical outcomes of larger lesion compared to smaller lesion treated with HTO.<sup>29,30</sup> A study by Goshima et al which reported open-wedge HTO has found that the treatment significantly improved weight-bearing line ratio (WBLR) and Japan Orthopedic Association (JOA) score with no adverse complications and revision surgery after 2 years of follow up.<sup>31</sup> However, varus deformity could impair healing process of necrotic lesions and increase risk of revision surgery.<sup>32,33</sup> Therefore, HTO was recommended to be done in SONK patients with small to medium lesion, without varus deformity.

OAT works with transplanting multiple cylindrical osteochondral grafts originating from peripheral area of less weight-bearing articular surface to defected cartilage.<sup>34</sup> Some studies showed greater clinical outcomes of OAT alone compared to microfracture for focal osteochondral and chondral defects among weight-bearing area.<sup>35,36</sup> However, varus knee deformity which could be seen in cartilage lesion of medial femoral condyle, could jeopardize success rate of OAT alone. Therefore, OAT could be in conjunction with HTO. A study by Minzlaff et al reported that survival rate on varus malalignment ( $>2^\circ$ ) which were treated with OAT+HTO after five years, seven years, and 8.5 years were 95%, 93%, and 90%, respectively. Same study also reported that the procedure could improve patients' satisfaction and clinical outcome significantly in larger varus deformity ( $>5^\circ$ ).<sup>37</sup> OAT also gave great results for larger lesion, even above  $4\text{ cm}^2$ .<sup>38-41</sup> A study by Kotani et al also described that OAT showed great functional score improvement regardless of age.<sup>42</sup> The same result was reported by Tarumi which studied administration of OAT+HTO on SONK of various ages.<sup>43</sup> Therefore, it could be concluded that OAT+HTO was a great choice for SONK surgery which provided efficacy and safety regardless of severity and age.

UKA was a surgery aimed at preserving the bony structure of the knee and to prevent micro damage. There were various reports of UKA success for SONK. A study by Parratte et al showed that UKA had a 12-year survival rate of 96.7%.<sup>44</sup> Another study by Langdown et al reported no failure of UKA within five years of treatment.<sup>45</sup> Study by Heyse et al which conducted UKA into 52 patients with follow up of 10.9 years founded that UKA significantly improved the American Knee Society (AKS) score with great satisfaction rate.<sup>46</sup> However, there was controversy between UKA and TKA. A study by Radke et al showed that TKA gave better clinical outcome when compared to UKA with UKA had 16.4% of 5-year failure rate.<sup>47</sup> Another study by Marmor et al founded 16.4% 5-year failure rate.<sup>48</sup> These findings were contradicted by Myers et al which found that UKA showed unfavorable outcome due to inappropriate selection of patients. It was also founded that UKA gave better safety due to its lower invasiveness, lower bone stock, and ability to preserve knee kinematics.<sup>13</sup> Due to those reasons and its effectivity, UKA was highly considered to be conducted in most of advance stage SONK cases.

This systematic review was the first to compare surgical methods for SONK. However, variability of outcomes limited this study to proceed to quantitative analysis. Therefore, more high quality randomized-controlled trials should be conducted to make meta-analysis possible, hence providing better evidence towards clinical care and research.

## CONCLUSION

Surgical approaches, which consisted of various methods (osteochondral autograft transplantation with concomitant high tibial osteotomy, high tibial osteotomy, total knee arthroplasty, and unicompartmental knee arthroplasty) provided good efficacy and safety towards patients with spontaneous osteonecrosis

of the knee, regardless of the methods used, hence could be considered as choice of option for patients at advance stage of the disease.

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