How long does a hip-preserving surgery with vascularized pedicle iliac bone grafts for femur head necrosis last? A systematic review and meta-analysis of case series with an average more than 5-year follow-up

CURRENT STATUS: POSTED

Xingyang Zhu
Guangzhou University of Chinese Medicine

Haitao Zhang
Guangzhou University of Chinese Medicine

Xiaobo Sun
Guangzhou University of Chinese Medicine

Yuqing Zeng
Guangzhou University of Chinese Medicine

Feilong Li
Guangzhou University of Chinese Medicine

Jinlun Chen
The First Affiliated Hospital of Guangzhou University of Chinese Medicine

Peng Deng
The First Affiliated Hospital of Guangzhou University of Chinese Medicine

Pengcheng Ye
The First Affiliated Hospital of Guangzhou University of Chinese Medicine

Yirong Zeng
The First Affiliated Hospital of Guangzhou University of Chinese Medicine

15713973727@126.com Corresponding Author

DOI:
10.21203/rs.2.24320/v1
SUBJECT AREAS
Orthopedics

KEYWORDS
ONFH, Iliac bone grafting, Total hip arthroplasty
Abstract

Background: Hip-preserving surgeries with vascularized pedicle iliac bone grafts (VPIBG) are effective for osteonecrosis of the femoral head (ONFH). However, few studies exist about the long-term efficacy of this procedure. The aim of this meta analysis was to investigate how long does this hip-preserving surgery last.

Methods: A comprehensive search was carried out through PubMed, Embase and Cochrane Collaboration Library for all relevant studies up to November 2019. The literature search strategy contained Medical Subject Headings and terms relating to ONFH and bone transplantation. All included studies were articles on VBIPG for ONFH, with an average follow-up of more than 5 years. Interesting outcomes included clinical success rates, complications, and conversion rates of THA. The data from eligible studies were then extracted and synthesized. The pooled effect size (ES) and 95% confidence intervals (CIs) were calculated.

Results: Ten studies were finally selected. Eight studies including 3413 hips were pooled into the meta-analysis of success rates, the overall ES was 0.89 (95% CI, 0.86–0.92). In subgroup analysis, the ES was 0.88 (95% CI, 0.78–0.98) and 0.90 (95% CI, 0.87–0.92) at an average 5-10 years and 10-15 years follow-up, respectively. Pooled analysis of THA conversion rates derived from 7 studies (3389 hips) showed the overall ES of 0.10 (95% CI, 0.09–0.11). Seven studies (3396 hips) were included in a meta-analysis of complication rates, and the overall ES was 0.12 (95% CI, 0.08–0.18). The most common complications were secondary wound healing (37.6%), numbness or paresthesia of the lateral thigh (22.4%), and deep vein thrombosis (19.6%).

Conclusions: The hip-preserving surgery with VPIBG is a safe and effective treatment for early-stage ONFH, but it should be used with caution in the treatment of advanced femoral head necrosis. The pooled data from this study suggested that 90% of the hips in patients with ONFH lasted 10 years after this surgery. However, most of the included studies are case series, and these conclusions will need the support of high-quality research in the future.

Introduction

Osteonecrosis of the femoral head (ONFH) is a common catastrophic disease [1, 2]. There are about 5
to 7.5 million patients in China with an annual increase of about 150,000 to 200,000 [3]. ONFH mainly affects young individuals and often involves bilateral hips [4, 5]. If treatment is not prompt and effective, 80% of ONFH will gradually progress to femoral heads collapse within 1 to 4 years, eventually leading to advanced osteoarthritis and even disability [3, 6]. Early diagnosis and aggressive treatment should be taken to arrest progression of ONFH [2], because once the femoral head collapses ≥ 4 mm or secondary osteoarthritis occurs, most patients have to receive total hip arthroplasty (THA) [3, 7]. However, THA is not the best choice for young patients due to the uncertainty of long-term survivorship of the prosthesis [5, 8]. Therefore, it is necessary to seek effective treatments to preserve the femoral head and to delay or avoid THA.

Currently, hip-preserving surgeries for ONFH mainly included core-decompression [9, 10], vascularized or non-vascularized bone grafting [1, 6, 11, 12], and osteotomy of the femur or acetabulum [13–15]. Hip-preserving surgery with vascularized pedicle iliac bone grafting (VPIBG) is an effective treatment for ONFH, which can reduce the intraosseous pressure, promote the revascularization of ischemic areas, provide structural support to prevent collapse [5, 16–18], and can be easily implemented without microsurgery techniques.

The VPIBG was proven to have good short-term outcomes [8, 19], but its medium to long-term results are still uncertain. The aim of this systematic review and meta-analysis was to answer the question of how long does a hip-preserving surgery with VPIBG for ONFH last.

Methods
This current systematic review and meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [20]. The research protocol had not been registered and ethical approval was not required, because this study just involved review of published literature, without involving the new patient data. Before starting the literature search, all coauthors agreed to the protocol.

Search Strategy
A comprehensive search of all relevant studies up to November 2019 was carried out through PubMed, Embase and Cochrane Collaboration Library. In addition, a manual search of possibly
relevant bibliographies was also conducted for additional citations. The literature search strategy contained Medical Subject Headings and terms related to ONFH and bone transplantation without language restrictions. The detailed search strategy is shown in appendix 1.

Inclusion And Exclusion Criteria
The following inclusion criteria were used. (1) All hip-preserving surgeries for ONFH were performed with VPIBG, and the average duration of follow-up must be greater or equal to 5 years. (2) The patient’s basic information (age, gender, etiology, stage of ONFH, etc.) had been recorded. (3) Outcomes (clinical success rate, radiographic progression, and secondary operations, etc.) were shown in detail. (4) Sufficient data was provided to calculate the pooled effect size (ES) with a 95% confidence interval (CI). (5) Specific information on postoperative rehabilitation as well as the perioperative complications was available.

The exclusion criteria were listed as follows. (1) The data of interest were incomplete. (2) Studies with an average follow-up of less than 5 years. (3) Clear definition of clinical failure was not given. (4) Repeated studies of the same patients at different periods. (5) Full manuscript was not available. (6) The language was not available for authors. (7) Reviews, case reports, commentaries and letters were also excluded.

Study Quality Assessment
The quality of the included case series studies was assessed using a quality appraisal checklist developed by the Institute of Health Economics (IHE), which evaluates bias from 20 criteria [21]. The quality of each study was assessed by answering “yes”, “partial”, “no”, or “unclear”. “Partial” responses were considered “yes”, while “unclear” responses were considered “no”. Finally, the number of “no” was calculated for estimating the risk of bias. As reported in a previous research [22], studies with 0-2 “no” responses were defined as low risk, 3-5 “no” responses were defined as moderate risk, 6-8 “no” responses were defined as high risk, and ≥ 9 “no” responses were defined as very high risk of bias. For case-control studies, the Newcastle-Ottawa Scale (NOS) was used [23]. The studies were evaluated by two reviewers independently, and controversies were resolved through discussions or the final decision was made by the third author.

Data Extraction
Relevant information were extracted by two reviewers independently from all selected studies with a standardized data collection form, which included the following variables: author, year of publication, country, average age, number of ONFH and patients, study type, etiology, stage of ONFH, and kinds of pedicle bone flap/size etc. The interest outcomes of our study included follow-up periods, rates of clinical success, numbers of conversion to THA, definitions of clinical failure, complications, loss to follow-up, as well as rates of radiographic progression. For studies that lacked the results we needed, we had done our best to contact the authors for more information. If any discrepancy between the 2 reviewers (Xingyang Zhu and Xiaobo Sun) during this process, they could reach consensus through discussion or seek help from the third author.

Statistical Analysis
The extracted raw data were used to calculate clinical success rate, THA conversion rate and complication rate. All statistical analyses were done with the Stata software (14.0) and P value < 0.05 was considered to be statistical significance. Each series was weighted according to its standard error (calculated from published CIs). The $I^2$ statistics and Chi square test were performed to estimate the heterogeneity size across studies. If heterogeneity test expressed $P > 0.1$ and $I^2 < 50\%$, data were pooled by a fixed-effects model, while the random effects was suitable for significant heterogeneity ($P \leq 0.1$ or $I^2 \geq 50\%$). Sensitivity analysis was conducted to determine the stability of the outcomes if it was necessary, and subgroup analysis was conducted to explore more specific information when the data were available. Forest plots were applied to depict the results of each studies and to evaluate pooled estimates, while the funnel plots were used to assess publication bias.

Results
Search Results
The initial search returned 1438 potentially relevant articles from the 3 databases. Four hundred and four duplicates were deleted, leaving 1034 articles for screening. Nine hundred and eighty three irrelevant citations were excluded after screening titles and abstracts by both reviewers, and 51 full-text papers remained for review. Another 41 studies were rejected for several reasons, such as other surgical methods ($n = 17$), lack of raw date ($n$
short follow-up (n = 9), duplicate research (n = 3), commentary, case reports or review (n = 5), inaccessible language (n = 1). Finally, 10 references were included in this study [16-18, 24-30]. The details of study selection process can be found in the Fig. 1.

**Study Characteristics And Quality**

Nine retrospective case-series studies and one retrospective case-control study, including 3042 patients (3481 hips), were finally selected [16-18, 24-30]. All studies were single center [16, 17, 24-30] except one multicenter study [18]. The main features of the included studies are shown in Table 1 and Table 2.
| Author/Year/Country | Study Design | Average age (years) | Gender M/F | Number of patients/hips (follow-up) | Classification system | Stage | Etiology (hips) | Follow-up time (year) | Validity of the studies |
|---------------------|--------------|---------------------|------------|------------------------------------|------------------------|-------|----------------|-----------------------|-------------------------|
| Eisenschen/2001/Germany | retrospective case series | NM | 81/21 | 90/90 | ARCO | NV | trauma(22)/alcohol(20)/steroids(12)/idiopathic(16)/sickle cell anemia(1) | 5 (0.5–10) | H |
| Xie/2019/China | retrospective case series | 38.01 ± 9.43 | 575/281 | 856 /1006 | Ficat and Arlet | II(575)/III(382)/IV(49) | steroid(383)/alcohol abuse(378)/traumatic(159)/idiopathic(87) | 15(5–25) | M |
| Hasegawa/2003/Japan | retrospective case-control | 37.9 (25–53) | 23/3 | 26/31 | * | II(28)/III-A(3) and I-B(1)/III-C(25)/IV(4)/II-1-B(1) | 13 (10–15) | 8(NOS) |
| Zhao/2017/China | retrospective multicentre case series | 43.15 ± 9.14 | 1364/826 | 1912/2179 | Ficat and Arlet | III(1733)/III(376)/IV(181) | Alcoholic(747)/steroid(497)/idiopathic(231)/traumatic(720) | 12 (5–25) | M |
| Ishizaka/1997/Japan | retrospective case series | 33(15–66) | 16/8 | 24/31 | Ficat and Arlet | II(18)/III(13)/IV(6) | steroid(17)/alcohol(10)/idiopathic(4) | 6 (2–11) | H |
| Leung/1996/China | retrospective case series | 32(24–52) | 12/6 | 18/21 | Myer’s classification | III(6)/IV(8)/V(7) | idiopathic(8)/alcoholic(3)/steroid(7)/posttraumatic(3) | 5 (5–12) | H |
| Babhulkar/2009/India | retrospective case series | 32(18–52) | 26/5 | 31/31 | ARCO | IIB(9)/IIC(22) | alcohol(16)/corticosteroid(12)/idiopathic(3) | 8(5–8) | M |
| Chen/2009/China | retrospective case series | 37(23–64) | 31/1 | 32/33 | ARCO | IIIA(26)/IIIB(7) | alcohol(27)/idiopathic(5)/steroid(1) | 5.8(0.7–13.8) | M |
| Pavlovicic/1999/Slovenia | retrospective case series | 38(25–55) | 23/1 | 24/24 | Ficat | II(7)/III(17) | idiopathic(12)/alcohol abuse(8)/traumatic(2)/steroid use(2) | 12.2(9–14) | H |
| Nagoya/2004/Japan | retrospective case series | 35(17–62) | 20/9 | 29/35 | ARCO | II(28)/III(7) | steroid(14)/alcohol(10)/idiopathic(5) | 8.6 (3–17) | M |

ARCO, Association Research Circulation Osseous; M, moderate risk; H, high risk; NM, not mention; NV, not available; *modified Inoue and Ono classification and the Japanese Investigation Committee; NOS, Newcastle-Ottawa Scale
| Author/ Year | Kinds of pedicle bone flap/Size(cm) | Duration of the operation | Postoperative management | defined clinical failure |
|--------------|----------------------------------|---------------------------|--------------------------|-------------------------|
| Eisenschen/ 2001 | vascular pedicled iliac crest with DICA /6 × 2 | NM | Nonweight bearing for 6 months | NM |
| Xie/ 2019 | vascular iliac bone grafting with ALCA/5 × 3 | 65(55–100) minutes | Non-weight bearing in the first 6 weeks, full weight bearing 6 months postoperatively | Conversion to THA or any other hip-preserving surgery |
| Hasegawa/ 2003 | vascular iliac pedicle bone graft with SICA (n = 23) or DICA (n = 8)/5 × 1.5 | NM | Ambulation was not permitted in first 3 weeks, partial weight-bearing from 12 weeks, full weight-bearing from 24 weeks | An clinical score of less than 70 points or conversion to THA |
| Zhao/ 2017 | one-sided cortical pedicled iliac bone flap with ALCA /2.5 × 2.5 | NM | Nonweight bearing in the first 6 weeks, full weight bearing 6 months postoperatively | Conversion to THA or any other hip-preserving surgery |
| Ishizaka/ 1997 | tricortical vascularized pedicle iliac bone block with DICA/2 × 2 × 5 | 2.5 hours | Nonweight bearing for 6 months, partial weight bearing for the next 6 months | Progressive collapse of 2 mm or more, or with osteoarthritic changes. |
| Leung, P/1996 | a iliac crest bone with DICA /NM | NM | Bed rest for 3–4 weeks, nonweight-bearing walking at the 4 week, weight-bearing until 8 weeks | Converted to THA |
| Babhulkar/2009 | part of iliac crest with DICA/NM | NM | The patients were mobilized after 15 days in bed, and after 4–6 weeks, patients were mobilized out of bed on non-weight bearing | NM |
| Chen/2009 | a tricortical vascularized iliac bone block with DICA /1.5 × 5 | NM | Toe-touch weight-bearing for the first 6 weeks, then progressive weight-bearing was permitted, full weight-bearing after 6 months | Conversion to TKA and radiographic failure as progressive femoral head collapse or secondary osteoarthritis |
| Pavlovci/1999 | a vascularized iliac crest bone graft with DICA /2 × 5 | NM | Passive hip movement started 3 to 4 days, full weight bearing 6 months later | Collapse of the femoral head within 3 years postoperatively |
| Nagoya/2004 | vascularized iliac bone graft perfused by DICA /NM | NM | Bed rest for 2 weeks, partial weight bearing for the next 6 months | Collapse occurred or progressed |

Nine case series studied had moderate to high risks of bias according to IHE [16–18, 24, 25, 27–30], while the case-control study obtained 8 scores based on NOS [26]. The validities of included studies are summarized in Appendix 2 and Appendix 3.

**Nutrient Vessels Of The Bone Flap**

The nutrient vessels of the iliac bone flap used by eligible studies contained DICA, ALCA and SICA. Seven studies used DICA [16, 24, 25, 27–30], two studies used ALCA [17, 18], and the remaining one used DICA or SICA [26]. Two studies reported the average length of operation, in which one took 65(55–100) minutes with ALCA bone
grafting [17], and the other spent about 2.5 hours with DICA bone grafting [29]. The remaining studies did not mention it.

Fixation Of The Bone Flap
Only 5 studies provided information about the fixation of bone grafts [16, 25, 28–30]. The bone block was secured by an additional screw [25] or by taking the stitch through the hole prepared by drilling in the neck and graft [16], while additional fixation was not applied in the remaining studies [28–30].

Clinical Evaluation
Clinical outcomes were evaluated by the following methods: Harris hip score (HHS) [16–18, 24, 26, 27], Japan Orthopaedic association hip (JOA) score [25], Merled’ Aubigne and Postel score (MP score) [29], and Charnley’s scoring system [30].

Postoperative Management
As shown in Table 2, all studies elaborated on postoperative management. Patients were generally recommended to begin toe-touch weight-bearing in the first 6 weeks after surgery, maintain partial weight-bearing for the next 6 weeks, and start complete weight-bearing after 3 to 6 months.

Definitions Of Clinical Failure
Various studies followed different definitions of clinical failure. Seven studies considered “conversion to THA or any other hip-preserving surgery” or “collapse of the femoral head and poor clinical function of the hip” as end points [17, 18, 24, 26, 28–30]. One study defined “femoral head collapse or progress of ONFH” as a failure [25]. And the remaining two studies did not give specific definitions [16, 27].

Clinical Outcomes
The average age of included patients was approximately 41.2 (15–66) years (excluding the study by Eisenschen [27]), and the male took up approximately 71.4%. The etiology mainly comprised alcohol abuse (35.5%), steroid use (27.3%), trauma (26.0%), Idiopathic (10.7%), and other (0.5%). The severity of ONFH was classified by different grading systems. Four studies used the Ficat classification [17, 18, 28, 29]. Four studies used the Association Research Circulation Osseous (ARCO) classification [16, 24, 25, 27]. And the remaining 2 studies used Myer’s classification [30], Inoue and Ono classification as well as Japanese Investigation Committee (JIC) classification [26], respectively. The maximum average follow-up period was 15 (5–25) years [17], and the minimum average period was 5 (0.5–10) years [27].

Success Rate Of Hip-preserving Surgery With VPIBG
The random-effects model was used because of the heterogeneity ($I^2 = 67.3\%$, $P = 0.003$). A total of 3413 hips in 8 studies were pooled into the meta-analysis of clinical success rates [16–18, 26–30], which showed that the overall ES was 0.89 (95% CI, 0.86–0.92), and the ES in subgroup analysis were 0.88 (95% CI, 0.78–0.98) and 0.90 (95% CI, 0.87–0.92) at an average follow-up of 5–10 years and 10–15 years, respectively, as shown in Fig. 2. Funnel plots illustrating the meta-analysis of clinical success rates indicated no obvious publication bias (Fig. 3).

The remaining 2 studies [24, 25] were not suitable for merger because of different inclusion criteria [24] or definition of clinical failure [25], and therefore were given a descriptive analysis. One study reported a success rate of 24.20% [24], which might be associated with all the included subjects who were ONFH patients with segmental collapse, because the well defined indications for this operation were those with precollapsed or early collapsed stage [5, 31]. The other study reported a success rate of 45.70%, which might be related to the study’s definition of failure as “femoral head collapse or progress of ONFH” [25]. This was because a proportion of patients, who showed radiographic progression after hip-preserving surgery and whose HHS improved significantly, did not need to receive THA subsequently [32]. Therefore, these patients should not be considered clinical failures. Given all the above reasons, data of these 2 studies were not merged in the meta analysis.

Clinical outcomes of each studies are shown in the Table 3.

| Author/ Year | Score system | Score (M ± SD) | outcomes | Clinical success rate | Complications/ (rate%)/lost follow-up | Complications/ (rate%)/lost follow-up |
|--------------|--------------|----------------|----------|-----------------------|---------------------------------------|---------------------------------------|
| Eisenschen/ 2001 | HHS | NM | 89 | conversion to THA(8 ) within 5 years, good or excellent(71) | 78.90% | 2 deep thrombosis of the femoral vein, 7 paresthesia and pain at the donor defect, 5 abdominal weakness, and 2 secondary wound healing/16 (17.7%) | died (5)/moved abroad(2)/lost followup(5) |
| Xie/ 2019 | HHS | 66.42 ± 6.52 | 87.43 ± 6.42 | 105 hips were converted to THA | 89.60% | 23 deep venous thrombosis, 16 meralgia paresthetica (which resolved), 47 secondary wound healing/86 (8.5%) | 75 patients (101hip) lost to follow-up, including 25 patients (32 hips) who died |
| Engineer/ Year | Score | Mean | SD | Rate Of Conversion To THA | Complications                                                                 |
|---------------|-------|------|----|---------------------------|-------------------------------------------------------------------------------|
| Hasegawa/2003 | HHS   | 69±9 | 83±8 | conversion to THA(2), 1 within 1 year and another at 9 years after surgery | 3 surgical wound necrosis, 8 irritation of the lateral femoral cutaneous nerve/11(35.5%) |
| Zhao/2017     | HHS   | 66.54±6.05 | 83.63±5.03 | converted to THA(215), including stage II (19), stage III (162), stage IV (34), no radiographic osteonecrotic progress(178) | 25 deep venous thromboses, 16 sensory deficits, 40 superficial infection and hematoma, 47 wound dehiscence/128 (5.9%) |
| Ishizaka/1997 | MP    | 13.5 | 15.7 | revised operations(3), satisfactory(24) | 77.4%                                                                        |
| Leung, P/1996 | Charnley | NA | NA | converted to THA(1), heaviness and weakness in the involved hips(7) at 2 years after operative after prolonged walking | 95.20%                                                                       |
| Babhulkar/2009| HHS   | 52.52±5.08 | 80.71±6.70 | 1 from stage III converted to THA | 1 superficial infection/1(3.2%) |
| Chen/2009     | HHS   | 62a | 80a | converted to TKA(25), mean survival time of the preserving-hip was 74 (44–95) months | 24.20%                                                                       |
| Pavlovicic/1999| NA   | NA | NA | poor results(8), fair results(6), hips good results(5), excellent results(5) | 66.70%                                                                       |
| Nagoya/2004   | JOA   | 50.9b/49.8c | 58.1b/79.2c | 19 hips collapse, 16 hips no collapse.16 of 28 stage 2 hips not collapse, in all 7 stage 3 hips collapse | 45.70%                                                                       |

M, mean difference; SD, standard deviation; HHS, Harris hip score; NM, not mentioned; NA, not available; JOA, Japanese Orthopaedic Association score; MP, Merled’ Aubigne and Postel score; a The score for the 8 hips that were preserved by the surgery(not containing 25 hips that convert to TKA); b the mean score for the hips that subsequently collapsed; c the mean score for the hips without collapse

**Rate Of Conversion To THA**

Pooled analysis of THA conversion rates derived from 7 studies (3389 hips) showed the overall ES of 0.10 (95%
with the fixed-effects model ($I^2 = 8.5\%, P = 0.364$) [16-18, 26, 27, 29, 30], and showed the ES of 0.06 (95% CI, 0.03–0.10) and 0.10 (95% CI, 0.09–0.11) at an average follow-up of 5–10 years and 10–15 years in subgroup analysis, respectively (Fig. 4).

**Viability Evaluation Of Implanted Flap**

Viability evaluation of implanted flap was performed in 2 studies [16, 24]. One study showed that 9 patients underwent digital subtraction arteriography at the end of 12 weeks and all cases proved the patency of DICA. The study also showed that the grafted areas of the femoral heads were showed high uptake through bone scan in 6 other patients [16]. Another study evaluated 17 hips through postoperative magnetic resonance imaging (MRI) scans and found isointense signals relative to the normal marrow and gadolinium enhancement in the viable graft [24].

**Complications**

Seven studies reported 255 complications [16-18, 25-28], with rates ranging from 3.2% (1/31 hips) [16] to 35.5% (11/31 hips) [26]. The pooled analysis of complication rates derived from these 7 studies (3396 hips) showed the overall ES of 0.12 (95% CI, 0.08–0.18) with the random-effects model ($I^2 = 88.1\%, P = 0.00$), as shown in Fig. 5. The three most common complications were secondary wound healing (37.6%), numbness or paresthesia of the lateral thigh (22.4%), and deep venous thromboses (19.6%).

**Discussion**

This systematic review and meta-analysis included 10 independent studies that analyzed 3042 patients (3481 hips) with ONFH treated by VPIBG, and the pooled data suggested an overall success rate of 89% for over 5 years of follow-up. This result was different from that of Yang et al [5], Who believed that the short-term effect of this protocol was better than the long-term effect. In addition, we found that the success rate of this operation was comparable between 5–10 years (88%) and 10–15 years (90%) of follow-up, which might be because the failure of this procedure was mainly concentrated in the early postoperative phase [5]. A previous study reported similar findings that the failure often occurred within the first 3 years after surgery [28].

Although THA can provide excellent clinical results, it is not the best choice for young patients with ONFH because of its high possibility of multiple revisions in the future [10, 33–35]. Thus, many hip-preserving operative procedures to salvage the femoral head are in vogue for young individuals [32, 36–40]. VBIPG is one of these procedures and has been widely implemented, because it requires no special equipment and microsurgery
techniques with a short operation time compared to free vascularized pedicled bone flap transplantation [3, 16, 37], and it is more conducive to rebuilding the blood flow of femoral head than non-vascularized pedicle flap transplantation [3, 6, 16, 41].

Of note, ONFH in different stages has a completely different prognosis [42]. This operation is more suitable for patients in ARCO stage II or III A/B than patients in stage III C or stage IV [3]. Xie et. al [17] found that the 15-year survival rate of hips with stage IV after hip-preserving procedure was significantly decreased compared with Ficat stage II and III. Another study showed that only 8 hips (24%) were successfully preserved after the hip-preserving surgeries with VPIBG on 33 hips (in 32 patients) with segmental collapse; thus, the author did not advocate this operation for collapsed ONFH [24]. However, we could not analyze the influence of different stages on the prognosis by combining effect size, because different staging methods had been applied in different studies and not every original study provided the final treatment outcome for each stage.

The combined data showed that alcohol abuse was the leading etiological factor of ONFH (35.5%), followed by steroid use (27.3%), trauma (26.0%) and idiopathic (10.7%). Most of studies had showed that long-term survival of hip-preserving surgery was not related to different etiologies. Howerer, Xie et. al [17] found that the survival rate in the traumatic group was higher than that in the alcoholic, idiopathic, and glucocorticoid groups after a follow-up of 15 years, and the long-term survival rate was the lowest in the glucocorticoid group. Unfortunately, due to the lack of raw data on clinical outcomes after surgery of each causative factor, we were unable to analyze the prognosis of each etiological factor.

The lateral buttress of the femoral head, as the load-bearing region, plays an important role in hip-preserving surgery, and patients with complete lateral buttress of the femoral head usually had a better prognosis than patients whose lateral buttress was affected by ONFH [29]. For instance, one study showed that 13 of 17 hips had no collapse in patients with type C-1 (JIC) necrosis, and that 15 of 18 hips had collapse in patients with type C-2 necrosis [25].

Age is another factor that affects the outcome of surgery. A study discovered that the mean survival time of the hips in patients 45 years or older was shorter than that in patients younger than 45 years [17].

Differences between interventions in various studies must be noted. First, the source of nutrient blood vessels for the bone graft was different. Second, the bone flap was fixed by an additional screw [25] or by the stitching [16],
or by bone embedding technique without any additional fixation [28–30]. Finally, the position of the bone flap could also influence the outcome of the surgery. One study demonstrated that the closer the pedicle bone graft was inserted into the anterolateral normal subchondral bone of the femoral head, the better it could reduce the collapse of femoral head [25].

Several methods, such as angiography [16, 28, 29], digital subtraction angiography (DSA) [43, 44], single-photon-emission computed tomography (CT) [24] and SPECT/CT [45], had been reported to evaluate the blood supply of vascular pedicle graft both before and after operation. Babhulkar S et al [16] advocated that preoperative angiography should be routinely performed on each patient to assess the presence of the transplanted blood vessel and to avoid vascular mutations. Liu Y et al [43] performed DSA on 48 patients before and 6 months after the operation to evaluate hemodynamic changes in ONFH with iliac bone flaps from the ALCA. They found that the position of the ALCA was relatively constant prior to operation, and also found that 44 of the 48 patients had a good blood supply to the femoral head 6 months after the operation, while the remaining 4 patients eventually underwent TKA due to poor blood flow of the femoral head. Another study used SPECT/CT to evaluate the femoral head bone viability after surgery with vascular bone graft, and a progressive increase of femoral head uptake were observed in all cases [45].

The operation had a relatively high incidence of complications, but most of them were minor and hardly affected the surgical effect. Secondary wound healing, irritation of the lateral femoral cutaneous nerve, and deep venous thromboses are the three most common complications.

To the best of our knowledge, this is the first meta-analysis evaluating the medium to long-term outcome of the hip-preserving surgery with VPIBG, in which only studies with an average follow-up of more than 5 years were included. We noticed that a previous excellent systematic reviews of this procedure by Yang F et al [5], but they did not combine effect sizes, so it is difficult to know the final success rate of this operation.

The present study did have some limitations. First, the included studies were mostly case series, rather than RCT or case-control studies, so the overall qualities of the studies were relatively low. Second, as mentioned above, there exist slightly different interventions between various studies. Third, the pooled data could not be stratified by factors that might affect survivorship, such as age, etiology factors, stage of ONFH, or location of necrotic zone, because these detailed data were not provided in each study. Fourth, although the mean follow-up of all
included studies was greater than 5 years, three of them also included cases with a follow-up of less than 5 years [16, 27, 29]. Finally, the studies had been implemented for a long time in different countries and had used different classification systems, interventions and efficacy criteria.

Conclusions
The findings of the present study indicated that the hip-preserving surgery with VPIBG was a safe and effective method for ONFH in ARCO stage II or III A/B, while it should be cautious when this method was used for ONFH in stage III C or IV. Although not enough information is yet available to tell us exactly how long this operation lasts, this study suggests that 90% of them last 10 years. Therefore, the medium to long-term effect of this operation is satisfactory. However, the included studies were mostly case series, high-quality studies are needed in the future.

Abbreviations
ONFH: Osteonecrosis of the femoral head; VPIBG: Vascularized pedicle iliac bone grafts; ARCO: Association Research Circulation Osseous; CIs: confidence intervals; ES: effect size; DICA: deep iliac circumflex artery; ALCA: ascending branch of the lateral circumflex artery; SICA: superficial iliac circumflex artery; HHS: Harris Hip Score; THA: total hip arthroplasty

Declarations
Acknowledgments
One of the first authors (Xingyang Zhu) want to show heartedly thanks to his wife Xiaoyang Si, who provided much help for grammar expression.

Funding
The article received financial support from the High-Level University Construction Project of Guangzhou University of Chinese Medicine (A1-AFD018171Z11068).

Availability of data and materials
Not applicable.

Author Contributions
Conceptualization: ZXY, ZYR. Literature review and search: ZXY, ZHT. Data collection: SXB, ZYQ. Data analysis and interpretation: LFL, CJL, YPC. Manuscript preparation & editing: ZXY, ZHT. Supervision: DP, ZYR. All authors have read and approved the manuscript.

Ethics approval and consent to participate
This was not required for this article.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that there are no conflicts of interest.

**Author details**

1 The First Clinical Medical School, Guangzhou University of Chinese Medicine, Jichang Road 12#, District Baiyun, Guangzhou, Guangdong, China. 2 Third Department of Orthopaedics, Yichuan People’s Hospital, Jiuchang Road 21#, Luoyang, Henan, China. 3 Third Department of Orthopaedics, The First Affiliated Hospital of Guangzhou University of Chinese Medicine, Jichang Road 16#, District Baiyun, Guangzhou, Guangdong, China.

**References**

1. Feng W, Chen J, Wu K, Lu L, Deng P, Ye P, et al. A comparative study of cortico-cancellous iliac bone graft with or without the combination of vascularized greater trochanter flap for the management of femoral head osteonecrosis: A minimum 6 years follow-up. BMC Musculoskeletal Disorders. 2019; 20(1).

2. Taha HM, Khan U. The descending branch of the lateral circumflex femoral artery: A reliable and robust alternative blood supply in the free fibular transfer for avascular necrosis of hip. European Journal of Plastic Surgery. 2012; 35(10):731-734.

3. Li Z. Scientific diagnosis and treatment of femoral head necrosis. Chinese Journal of Reparative and Reconstructive Surgery. 2005; 19(9):685-686.

4. Zeng YR, He S, Feng WJ, Li FL, Li J, Jian LY, et al. Vascularised greater trochanter bone graft, combined free iliac flap and impaction bone grafting for osteonecrosis of the femoral head. Int Orthop. 2013; 37(3):391-398.

5. Yang F, Wei Q, Chen X, Hong G, Chen Z, Chen Y, et al. Vascularized pedicle iliac bone grafts as a hip-preserving surgery for femur head necrosis: a systematic review. Journal of orthopaedic
surgery and research. 2019; 14(1):270.

6. Sultan AA, Khlopas A, Surace P, Samuel LT, Faour M, Sodhi N, et al. The use of non-vascularized bone grafts to treat osteonecrosis of the femoral head: indications, techniques, and outcomes. International Orthopaedics. 2019; 43(6):1315-1320.

7. Gasbarra E, Perrone FL, Baldi J, Bilotta V, Moretti A, Tarantino U. Conservative surgery for the treatment of osteonecrosis of the femoral head: current options. Clinical cases in mineral and bone metabolism: the official journal of the Italian Society of Osteoporosis, Mineral Metabolism, and Skeletal Diseases. 2015; 12(Suppl 1):43-50.

8. Elmali N, Ertem K, Karakaplan M, Pepele D, Daggez C, Topgul H. Vascular pedicled iliac bone grafting is effective in patients with an early stage of femoral head avascular necrosis. Eklem Hastalik Cerrahisi. 2014; 25(1):2-7.

9. Hua KC, Yang XG, Feng JT, Wang F, Yang L, Zhang H, et al. The efficacy and safety of core decompression for the treatment of femoral head necrosis: a systematic review and meta-analysis. Journal of orthopaedic surgery and research. 2019; 14(1):306.

10. Cao P, Cai S, Dai C, Liu C, Niu Y, Wang X, et al. Multi-directional core decompression apparatus with impaction bone grafting for the treatment of femoral head osteonecrosis. International Journal of Clinical and Experimental Medicine. 2018; 11(10):10847-10855.

11. Millikan PD, Karas V, Wellman SS. Treatment of osteonecrosis of the femoral head with vascularized bone grafting. Current Reviews in Musculoskeletal Medicine. 2015; 8(3):252-259.

12. Ding H, Gao YS, Chen SB, Jin DX, Zhang CQ. Free vascularized fibular grafting benefits severely collapsed femoral head in concomitant with osteoarthritis in very young adults: a prospective study. J Reconstr Microsurg. 2013; 29(6):387-392.

13. Kubo Y, Yamamoto T, Motomura G, Karasuyama K, Sonoda K, Iwamoto Y. Patient-reported outcomes of femoral osteotomy and total hip arthroplasty for osteonecrosis of the femoral head: a prospective case series study. SpringerPlus. 2016; 5(1):1880.
4. Kawano K, Motomura G, Ikemura S, Kubo Y, Fukushima J, Hamai S, et al. Long-term hip survival and factors influencing patient-reported outcomes after transtrochanteric anterior rotational osteotomy for osteonecrosis of the femoral head: A minimum 10-year follow-up case series. Modern rheumatology. 2018;1-7.

5. Morita D, Hasegawa Y, Okura T, Osawa Y, Ishiguro N. Long-term outcomes of transtrochanteric rotational osteotomy for non-traumatic osteonecrosis of the femoral head. The bone & joint journal. 2017; 99-b(2):175-183.

6. Babhulkar S. Osteonecrosis of femoral head: Treatment by core decompression and vascular pedicle grafting. Indian journal of orthopaedics. 2009; 43(1):27-35.

7. Xie H, Wang B, Tian S, Liu B, Qin K, Zhao D. Retrospective Long-Term Follow-Up Survival Analysis of the Management of Osteonecrosis of the Femoral Head With Pedicled Vascularized Iliac Bone Graft Transfer. Journal of Arthroplasty. 2019; 34(8):1585-1592.

8. Zhao D, Xie H, Xu Y, Wang Y, Yu A, Liu Y, et al. Management of osteonecrosis of the femoral head with pedicled iliac bone flap transfer: A multicenter study of 2190 patients. Microsurgery. 2017; 37(8):896-901.

9. Cao H, Guan H, Lai Y, Qin L, Wang X. Review of various treatment options and potential therapies for osteonecrosis of the femoral head. Journal of Orthopaedic Translation. 2016; 4:57-70.

10. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010; 8(5):336-341.

11. Guo B, Moga C, Harstall C, Schopflocher D. A principal component analysis is conducted for a case series quality appraisal checklist. Journal of clinical epidemiology. 2016; 69:199-207.e192.

12. Hennequin-Hoenderdos NL, Slot DE, Van der Weijden GA. The incidence of complications associated with lip and/or tongue piercings: a systematic review. International journal of dental hygiene. 2016; 14(1):62-73.
3. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. European journal of epidemiology. 2010; 25(9):603-605.

4. Chen CC, Lin CL, Chen WC, Shih HN, Ueng SW, Lee MS. Vascularized iliac bone-grafting for osteonecrosis with segmental collapse of the femoral head. J Bone Joint Surg Am. 2009; 91(10):2390-2394.

5. Nagoya S, Nagao M, Takada J, Kuwabara H, Wada T, Kukita Y, et al. Predictive factors for vascularized iliac bone graft for nontraumatic osteonecrosis of the femoral head. Journal of orthopaedic science : official journal of the Japanese Orthopaedic Association. 2004; 9(6):566-570.

6. Hasegawa Y, Sakano S, Iwase T, Iwasada S, Torii S, Iwata H. Pedicle bone grafting versus transtrochanteric rotational osteotomy for avascular necrosis of the femoral head. The Journal of bone and joint surgery British volume. 2003; 85(2):191-198.

7. Eisenschenk A, Lautenbach M, Schwetlick G, Weber U. Treatment of femoral head necrosis with vascularized iliac crest transplants. Clin Orthop Relat Res. 2001; (386):100-105.

8. Pavlovic V, Dolinar D, Arnez Z. Femoral head necrosis treated with vascularized iliac crest graft. Int Orthop. 1999; 23(3):150-153.

9. Ishizaka M, Sofue M, Dohmae Y, Endo N, Takahashi HE. Vascularized iliac bone graft for avascular necrosis of the femoral head. Clin Orthop Relat Res. 1997; (337):140-148.

10. Leung PC. Femoral head reconstruction and revascularization. Clin Orthop Relat Res. 1996; (323):139-145.

11. Hasegawa Y, Iwata H, Torii S, Iwase T, Kawamoto K, Iwasada S. Vascularized pedicle bone-grafting for nontraumatic avascular necrosis of the femoral head. A 5- to 11-year follow-up. Arch Orthop Trauma Surg. 1997, 116; (5):251-258.

12. Wu CT, Yen SH, Lin PC, Wang JW. Long-term outcomes of Phemister bone grafting for patients
with non-traumatic osteonecrosis of the femoral head. International Orthopaedics. 2019; 43(3):579-587.

3. Ligh CA, Nelson JA, Fischer JP, Kovach SJ, Levin LS. The Effectiveness of Free Vascularized Fibular Flaps in Osteonecrosis of the Femoral Head and Neck: A Systematic Review. J Reconstr Microsurg. 2017; 33(3):163-172.

4. Zhou G, Zhang Y, Zeng L, He W, Pang Z, Chen X, et al. Should thorough Debridement be used in Fibular Allograft with impaction bone grafting to treat Femoral Head Necrosis: a biomechanical evaluation. BMC Musculoskelet Disord. 2015; 16:140.

5. Feng W, Ye P, Ni S, Deng P, Lu L, Chen J, et al. One-stage simultaneous hip-preserving surgeries for the management of bilateral femoral head osteonecrosis: a mean 7.0-year follow-up. Journal of orthopaedic surgery and research. 2019; 14(1):455.

6. Zhao D, Liu B, Wang B. Vascularized Greater Trochanter Bone Flap Transfer for Treatment of ARCO Stage-IIIB to IIIIB Osteonecrosis of the Femoral Head. JBJS Essential Surgical Techniques. 2019; 9(2).

7. Unal MB, Cansu E, Parmaksizoglu F, Cift H, Gurcan S. Treatment of osteonecrosis of the femoral head with free vascularized fibular grafting: Results of 7.6-year follow-up. Acta Orthop Traumatol Turc. 2016; 50(5):501-506.

8. Yildiz C, Erdem Y, Koca K. Lightbulb technique for the treatment of osteonecrosis of the femoral head. Hip international : the journal of clinical and experimental research on hip pathology and therapy. 2018; 28(3):272-277.

9. Luring C, Benignus C, Beckmann J. Joint-preserving operative treatment of avascular necrosis of the femoral head. Orthopade. 2018; 47(9):745-750.

10. Lu Y, Lu X, Li M, Chen X, Liu Y, Feng X, et al. Minimally invasive treatment for osteonecrosis of the femoral head with angioconductive bioceramic rod. Int Orthop. 2018; 42(7):1567-1573.

11. Chen L, Lin Z, Wang M, Huang W, Ke J, Zhao D, et al. Treatment of trauma-induced femoral
head necrosis with biodegradable pure Mg screw-fixed pedicle iliac bone flap. Journal of Orthopaedic Translation. 2019; 17:133-137.

2. Chen L HG, Fang B, Zhou G, Han X, Guan T, He W. Predicting the collapse of the femoral head due to osteonecrosis From basic methods to application prospects. J Orthop Translat. 2017; 11:62-72.

3. Liu Y, Zhao D, Wang WM, Wang BJ, Zhang Y, Li ZG. Hemodynamic changes in osteonecrosis treatment of the femoral head with iliac bone flaps pedicled with the lateral femoral circumflex artery ascending branch: A 10-year report. Technology and Health Care. 2016; 24:S493-S498.

4. Zhao D, Yu X, Wang T, Wang B, Liu B, Tian F, et al. Digital subtraction angiography in selection of the vascularized greater trochanter bone grafting for treatment of osteonecrosis of femoral head. Microsurgery. 2013; 33(8):656-659.

5. Fontecha CG, Roca I, Barber I, Menendez ME, Collado D, Mascarenhas VV, et al. Femoral head bone viability after free vascularized fibular grafting for osteonecrosis: SPECT/CT study. Microsurgery. 2016; 36(7):573-577.

Figures
Figure 1

Summary of the evidence search and selection process
| Study ID   | Forest Plot of Clinical Success Rate. 1, Average Follow-up of 5-10 Years; 2, Average Follow-up of 10-15 Years |
|-----------|----------------------------------------------------------------------------------------------------------|
| 1         | Eisenchen2001                                                                                           |
|           | 0.79 (0.70, 0.87)                                                                                       |
|           | 9.02                                                                                                     |
| 1         | Ishizaka1997                                                                                            |
|           | 0.77 (0.63, 0.92)                                                                                       |
|           | 3.68                                                                                                     |
| 1         | Leung, P1996                                                                                            |
|           | 0.95 (0.86, 1.04)                                                                                       |
|           | 8.06                                                                                                     |
| 1         | Babhulkar2009                                                                                            |
|           | 0.97 (0.91, 1.03)                                                                                       |
|           | 13.32                                                                                                    |
| 1         | Subtotal (I-squared = 80.3%, p = 0.002)                                                                 |
|           | 0.88 (0.78, 0.98)                                                                                       |
|           | 34.09                                                                                                    |
| 2         | Pavlovic1999                                                                                            |
|           | 0.67 (0.48, 0.86)                                                                                       |
|           | 2.35                                                                                                     |
| 2         | Xie2019                                                                                                 |
|           | 0.90 (0.88, 0.91)                                                                                       |
|           | 27.60                                                                                                    |
| 2         | Hasegawa2003                                                                                            |
|           | 0.90 (0.80, 1.01)                                                                                       |
|           | 6.58                                                                                                     |
| 2         | Zhao2017                                                                                                |
|           | 0.90 (0.89, 0.91)                                                                                       |
|           | 29.39                                                                                                    |
| 2         | Subtotal (I-squared = 50.8%, p = 0.107)                                                                 |
|           | 0.90 (0.87, 0.92)                                                                                       |
|           | 65.91                                                                                                    |
| 2         | Overall (I-squared = 67.3%, p = 0.003)                                                                  |
|           | 0.89 (0.86, 0.92)                                                                                       |
|           | 100.00                                                                                                  |

NOTE: Weights are from random effects analysis.
Figure 3

Funnel plot illustrating a meta-analysis of success rates. se, standard error; ES, effect size
| Study ID | ES (95% CI)          | Weight |
|---------|----------------------|--------|
| 1       |                      |        |
| Eisenschen2001 | 0.09 (0.03, 0.15)    | 2.87   |
| Ishizaka1997   | 0.10 (-0.01, 0.20)   | 0.92   |
| Leung, P1996   | 0.05 (-0.04, 0.14)   | 1.20   |
| Babhulkar2009  | 0.03 (-0.03, 0.09)   | 2.57   |
| Subtotal (I-squared = 0.0%, p = 0.533) | 0.06 (0.03, 0.10) | 7.55   |
| 2       |                      |        |
| Xie2019    | 0.10 (0.09, 0.12)    | 27.81  |
| Hasegawa2003 | 0.06 (-0.02, 0.15)   | 1.33   |
| Zhao2017   | 0.10 (0.09, 0.11)    | 63.31  |
| Subtotal (I-squared = 0.0%, p = 0.639) | 0.10 (0.09, 0.11) | 92.45  |
| Heterogeneity between groups: p = 0.063 |          |        |
| Overall (I-squared = 8.5%, p = 0.364) | 0.10 (0.09, 0.11) | 100.00 |

Figure 4

Forest plot of THA conversion rates. 1, average follow-up of 5-10 years; 2, average follow-up of 10-15 years
Figure 5

Forest plot of complication rates

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

Appendix.doc
PRISMA 2009 checklist.doc