


S3-Guideline non-traumatic adult femoral head necrosis

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Abstract

Introduction The treatment of adult non-traumatic avascular necrosis of the femoral head (AVN; N-ANFH) within an estimated incidence of 5000–7000 cases per annum in Germany remains a challenge. Risk factors include steroids, alcohol abuse, chemotherapy and immunosuppressive medication, but a genetic predisposition has been suggested. Early diagnosis of this often bilateral disease process is essential for successful conservative or joint

preserving surgical management. In this review, we present the update German consensus S3 guideline “diagnosis and management for N-ANFH” as a concise summary.

Materials and methods This systematic review is based on the published literature from January 1, 1970 to April 31, 2013 (German and English language). Inclusion criteria were systematic reviews, meta-analyses and relevant peer review publications. We identified a total of 3715 related

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publications, of which 422 were suitable according to the SIGN criteria, but only 159 fulfilled our inclusion criteria. **Results and conclusions** Clinical suspicion of N-ANFH mandates radiographic evaluation. If radiographs are normal MRI scans are recommended, which should be evaluated according to the ARCO-classification. Differential diagnoses include transient osteoporosis, bone bruise, insufficiency fracture and destructive arthropathy. Untreated, subchondral fractures commonly occur within 2 years, during which the risk for contralateral involvement is high—thereafter unlikely. Conservative management with Ilomedin and Alendronat can be tried, but other pharmacological or physical treatments are inappropriate. No specific joint preserving procedure can be recommended, but core decompression should be considered in early stages if necrosis is <30 %. In ARCO stages IIIc or IV total hip arthroplasty (THA) should be contemplated, which offers similar outcome compared to osteoarthritis. Young age is the main risk factor for higher revision rates after THA for N-ANFH.

Keywords Atraumatic avascular necrosis · AVN · Diagnosis · Ilomedin · Bisphosphonate · Core decompression · Bone grafting · Bone transplant · Total hip replacement · Total hip arthroplasty

Introduction

Non-traumatic avascular necrosis of the femoral head (N-ANFH) usually affects adults of young/middle age and occurs bilaterally. An increasing incidence of idiopathic cases has been reported, but steroid and immunosuppression therapy (e.g., transplant patients), alcohol misuse and chemotherapy remain important causes. Early diagnosis is essential to allow for joint preserving surgical management attempts. Femoral head collapse commonly occurs within 2 years after onset and necessitates total hip arthroplasty (THA).

The German S3 guidelines have been developed under the patronage of the German society for Orthopaedics and Traumatology (DGOOC) and the German societies of Radiology (DRG), of Physical Therapy and Rehabilitation (DGPMR) and Osteology (DVO). The up to date evidence was reviewed in 2013 in order to establish the current status of diagnosis and management of N-ANFH, both in terms of conservative/pharmacological and stage-dependent surgical management.

The purpose of this review to provide a concise summary of the originally in German published S3 guidelines in English to reach a wider readership. The full length S3 guidelines from 2014 (<http://www.awmf.org/leitlinien/detail/II/033-050.html>) give 38 evidence based recommendations, some of which

have already published in German sub-specialty journals [1–4].

Materials and methods

An extensive literature search of all topic relevant and related published articles was carried out using internet sites of the AWMF (“Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V.” or Association of the Scientific Medical Societies in Germany) [5], the “National Guideline Clearinghouse” and the “Guidelines International Network”, a further systematic literature search was done using the data bases of the US National Library of Medicine National Institutes of Health (<http://www.ncbi.nlm.nih.gov/pubmed>) and the Cochrane Library (www.cochranelibrary.com). The following keywords were used “Femur Head Necrosis” [Majr:NoExp] NOT “Legg-Perthes Disease” [Mesh] capturing the period from January 1, 1970 to May 31, 2013.

- The inclusion and exclusion criteria are presented in Table 1.
- A limitation to randomised studies was not feasible due to the lack of sufficient numbers and hence per reviewed publications of lower evidence level had to be included.
- The level of evidence (LoE) as defined by the Scottish Intercollegiate Guidelines Network (SIGN) [6] was applied.
- Furthermore clinical relevance, study endpoints, clinical applicability, patient preference and ethics and economic aspects were evaluated.
- For the expert consensus based recommendations (ER) the AMFW Grading System [AWMF 2012] was used: “A = must”, “B = should”, “O = may”.
- The strength of participating expert consensus (EC) was judged as “strong” (agreement >95 %) and “medium” (agreement 75–95 %).
- In cases of discrepancies between LoE and recommendation grade the specific reasons were stated in the original S3 guideline (<http://www.awmf.org/leitlinien/detail/II/033-050.html>).

Results

The search revealed a total of 3715 articles (1606 prior to 1991 and 2109 from 1991 to May 31, 2013), of which 422 were pre-selected. Based on the criteria set out in Table 1, a total of 159 articles (43 in relation to national history and conservative management, 72 in relation to diagnosis/imaging and 64 in relation to operative intervention) were included for detailed evaluation.

Table 1 Inclusion and exclusion literature search criteria (search period Jan 1, 1970–May 31, 2013)**Inclusion criteria**

Systematic reviews
 Meta-analyses
 Peer review articles/clinical studies
 Full text publications in German or English language

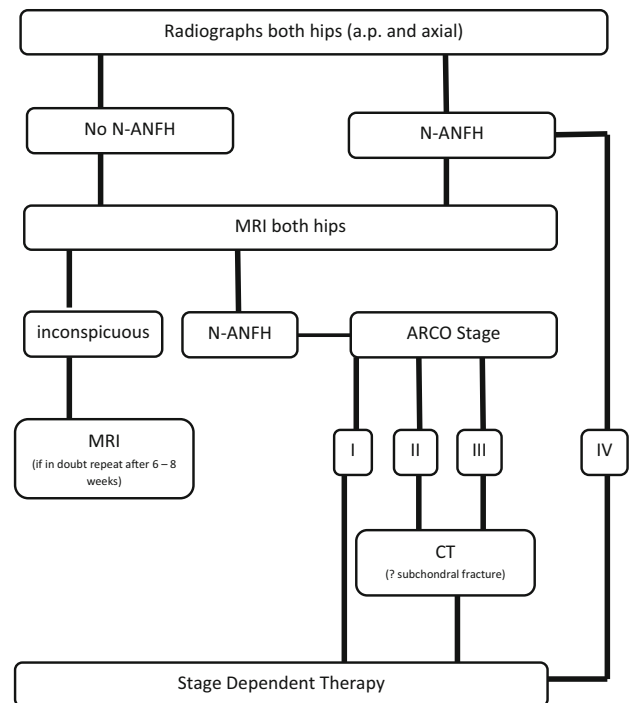
Exclusion criteria

Non-peer review article
 Second publication/duplication
 Editorials
 Letter to editor
 Comments
 Case series or case reports
 Infection, Perthes disease, slipped upper femoral epiphysis, trauma
 Animal experiment based studies
 Laboratory experimental studies (e.g., cell cultures)
 Outdated/obsolete diagnostic procedures (e.g., intra-osseous pressure measurements)
 Outdate/obsolete therapeutic procedures (e.g., implants no longer on market)

The relevant findings and conclusions are presented on a point-by-point basis with the respective level of evidence (LoE) and recommendation grade (EC). Relevant important literature is quoted where necessary.

Diagnosis of N-ANFH: imaging**Conclusions**

- In cases of clinical suspicion (groin pain and/or around hip/thigh >6 weeks, underlying known risk factors, antalgic limp, painful restriction of movement, absence of other cause/diagnosis) radiographs (pelvis ap and lateral hip/Lauenstein view) should be obtained (EC “strong”) [7–20].
- Radiographic grading using the ARCO classification is recommended (EC “medium”) [21–32]*.
- If radiographs are normal and symptoms persist an MRI scan of both hips due to potential bilateral disease should be requested (LoE 2++, ER B, EC “strong”) [15, 16, 18, 33–39].
- In radiographic stages ARCO 2 and 3 MRI scans are also recommended to determine area and extent of necrosis and to exclude/confirm subchondral fracture and collapse (LoE 2-3, ER B, EC “strong”) [21, 29, 40–51].
- In stage ARCO 2 a CT scan will aid to clarify the presence/extent of subchondral fracture if the MRI is inconclusive (LoE 2++, ER B, EC “strong”) [7, 52].

**Fig. 1** Stage-dependent use of imaging techniques in clinical suspicion of N-ANFH (according Reppenhagen [53])

- Bone scanning is not indicated (LoE 2++, ER 0, EC “strong”) [49–51].
- The algorithm (Fig. 1) proposed by Reppenhagen et al. (2007) is recommended to allow for timely and stage-dependent diagnostic assessment when suspecting N-ANFH (EC “strong”) [53].

Supporting evidence and further comments

*The ARCO classification [54] as outlined in Table 2 is based on the grading systems proposed by Ficat and Arlet [22], Steinberg et al. [24, 25] and also Ohzono et al. [27]. The original ARCO grading is primarily based on radiographs. Both MRI and CT scanning are helpful to better differentiate between stage 2 and 3 (“crescent”) sign, establish extent of necrosis and allow a more pragmatic and clinically relevant approach. Stage 0 has become obsolete as not clinically relevant.

Diagnostic challenges/differential diagnoses

- Transient osteoporosis of the hip (TOH) is an important differential diagnosis (DD). A diffuse oedema pattern on MRI may be seen in both entities, but a more patchy pattern and the absence of focal defects and subchondral changes is suggestive of TOH (EC “medium”) [55–69].

Table 2 Staging system of non-traumatic avascular necrosis of the femoral head (N-ANFH) according to Association Research Circulation Osseous (ARCO) Gardeniers [54]

Stage	Clinical presentation, pathology, imaging
0	Normal radiographs, MRI and bone scan—necrosis on histology
1	Normal radiographs/CT scan Pathological MRI or bone scan Sub-classification in relation to femoral head localisation (lateral, medial or anterior) and size/area of head necrosis (<15, 15–30, >30 %)
2	Radiographic structural changes of femoral head bony architecture without contour changes Normal joint space AVN typical MRI findings Sub-classification in relation to femoral head localisation (lateral, medial or anterior) and size/area of head necrosis (<15, 15–30, >30 %)
3	Radiographic structural femoral head changes with subchondral fracture (“crescent sign”) Femoral head flattening (<2, 2–4, >4 mm) Normal joint space Sub-classification in relation to femoral head localisation (lateral, medial or anterior) and size/area of head necrosis (<15, 15–30, >30 %)

- As other DD stress-/insufficiency fractures, osteonecrosis and destructive arthropathies should be considered (EC “medium”) [70–78].

Natural history/untreated N-ANFH and risk factors

- N-ANFH is a progressive disease and subchondral fractures and collapse femoral head usually occurs within 2 years, hence making hip joint preserving surgical intervention impossible. This is particularly the case in patients with bilateral involvement and uncontrollable factors/causes (LoE 2+/2++, EC “strong”) [36, 37, 39, 79–82].
- After diagnosis of unilateral N-ANFH the risk of contralateral N-ANFH is high within the first 2 years, but diminishes thereafter (LoE 2+/2++, EC “strong”) [41, 44, 45, 82, 83].

Conservative management

- Conservative treatment of N-ANFH alone does not provide prolonged symptomatic relief and does not prevent disease progression (LoE 2+/2++, EC “strong”) [79, 84].
- Pharmacological vasodilation with the prostacyclin analogon Iloprost can be considered in ARCO stages 1–2 for reduction of pain and bone marrow oedema in patients where surgical intervention is contraindicated or declined. Administration of Iloprost is considered as

off-label use and inappropriate when a subchondral fracture has already occurred (LoE 2+, ER 0, EC “strong”) [85–89].

- Bisphosphonates (Alendronate) with their bone resorption inhibitive properties have been shown to delay structural femoral head damage/collapse and to reduce levels of pain (LoE 2+, ER 0, EC “medium”) [36, 90–95].
- There is insufficient evidence to support the use of anticoagulant drugs (LMWH, Warfarin) and are hence not recommended (LoE 2+, ER A, EC “strong”) [96, 97].
- Statines do not reduce the risk for N-ANFH and are hence not recommended (LoE 2+, ER A, EC “strong”) [98, 99].
- Hyperbaric oxygen therapy (HBO) has been shown to improve tissue oxygenation, reduces oedema, induces angiogenesis and reduces intraosseous hypertension with improved microcirculation, but no evidence is available to show that femoral head collapse can be delayed. Currently the use of HBO is not recommended (LoE 2+, ER B, EC “strong”) [85, 100–102].
- There is no evidence to support that extracorporeal shock wave therapy (ESWT) and ultrasound may delay femoral head collapse and are hence not recommended (LoE 1, ER B, EC “strong”) [85, 103–107].
- Electrostimulation and pulsating electromagnetic fields (PEMF) may improve symptoms in early disease, but no evidence is available to show that femoral head collapse can be delayed. Their use in the treatment of N-ANFH is not recommended (LoE 2+, ER B, EC “strong”) [108–114].

Joint preserving operative interventions: timing, rationale and indications

- The evidence suggests that joint preserving operative procedures can be offered/tried in ARCO stage 1–3 (LoE: 2+, EC “strong”).
- No specific procedure can be identified as being superior. The type of surgery depends on the extent of femoral head involvement/necrosis (LoE: 2++, EC “strong”) [45, 115–119].
- Core decompression is indicated and should be offered in early and potential reversible stages of N-ANFH, i.e. ARCO 1, but also stage ARCO 2 (irreversible early stage) if the area of necrosis is medial or central and <30 %.(LoE 2++, ER A, EC “strong”).
- In ARCO 3 with infraction of the femoral head core decompression may be considered for short term symptomatic relief (LoE 2++, ER 0, EC “strong”) [36, 38, 79, 84, 88, 105, 108, 114, 120–126].
- Additional electric stimulation (in combination with core decompression) may improve pain, but does not improve radiographic outcome (LoE 2+, EC “strong”) [108, 112, 113, 127–129].
- Core decompression plus systemic Alendronate (off-label use) may reduce pain and disease progression compared to core decompression alone (LoE 2+, ER O, EC “medium”) [95].
- Core decompression plus bone grafting is not superior to core decompression alone, but both are superior to conservative management. [45, 123, 130–134]. Core decompression should only be offered if the area of necrosis is <20 % and if the Kerboul angle is <200° (LoE: 2+, ER B, EC “strong”).
- Vascularised fibular transplant/graft is technically demanding and is not recommended as a routine procedure and variable outcomes have been reported with small and larger defect/necrosis sizes. It may be offered in specialised treatment centres in younger patients with ARCO 1 and 2 (LoE 2+, ER B, EC “strong”) [122, 135–144].
- Osteochondral allografts cannot be recommended, as the outcome is not yet clear (LoE 3, ER B, EC “strong”) [145].
- Autogenous cancellous bone grafting cannot be recommended, as the outcome is not yet clear (LoE 2+, ER B, EC “strong”) [85, 130, 132].
- Corrective femoral osteotomies are accepted, but technically extremely demanding procedures and should only be considered/offered for younger patients in specialised treatment centres in early disease (LoE 2++, ER B, EC “strong”) [125, 146, 147].

- There is no scientific evidence for efficacy of Tantalum-implants and the avascular necrosis rod, which are not recommended (LoE 2+, ER B, EC “strong”) [148, 149].
- In stage ARCO 3c and 4, core decompression is not indicated and total hip replacement (THR) should be discussed (LoE 2++, ER B, EC “strong”) [36, 38, 79].

Total hip replacement: outcome and implant fixation

Results after primary THR and risk factors for revision

- Revision rates after THR for N-ANFH have significantly fallen since 1990 and are now similar to global failure rates reported nationally [122, 150–152].
- The short-, medium- and long-term results after THR for N-ANFH are comparable to outcome after THR for osteoarthritis [154–165].
- THR after preceding procedures, i.e., fibular graft and osteotomies, maybe more complex [153].
- All types and stages of femoral head necrosis can be treated successfully with THR, but less favourable clinical outcome has to be expected in alcohol or steroid related N-ANFH [153–156].
- The main risk factor for premature failure and re-operation/implant revision is the young patient age. The revision risk also seems to depend on the underlying aetiology: higher failure rates occur with sickle cell disease, Gauchers disease, renal failure or in patients after renal transplant surgery (LoE: 2+ to 2++, EC “strong”) [153–156].

Prosthesis type/mode of fixation

- Similar outcome can be expected after implantation of cemented and uncemented THR, both of which are recommended as the gold standard (LoE 2+ to 2++, ER B, EC “strong”) [153, 158, 160, 164, 165].
- Hip resurfacing in younger men (<55 years) can be considered if femoral head quality is adequate for implant fixation. Metal ion wear related complications must be discussed (LoE 2+ to 2++, ER 0, EC “strong”) [159, 160].
- No sufficient evidence currently exists to support recommendation of short femoral stem designs [153].

Compliance with ethical standards

Conflict of interest Potential conflict of interest statements have been declared and can be found online on pages 87–93 of the full

length German S3 guideline. (<http://www.awmf.org/leitlinien/detail/ll/033-050.html>). Prof. Andreas Roth: Advisory board Ceramtec, member of a study regarding measurement of periprosthetic bone density with Servier in 2012–2014. Johannes Beckmann: Referent for DePuy, Aesculap, ConforMIS and Brainlab, project together with ConforMIS 2006–2009. Prof. Dr. Klaus Bohndorf: Fee for a Symposium with Braun in 2013, shares from Boston Imaging Lab. Dr. Alexander Fischer: nothing. Prof. Christian Heiß: Advisory board Stryker, Aap and Biomet. Prof. Werner Kenn: nothing. Prof. Marcus Jäger: Reports, projects an fee from/with Braun, Aesculap and DePuy. Priv.-Doz. Dr. Uwe Maus: Fee from Lilly, Servier, Abb Vie and Amgen. Prof. Ulrich Nöth: Fee from Lilly, Servier, Abb Vie and Amgen. Prof. Klaus M. Peters: Fee from Amgen, Lilly, Servier, Humantis, shares from Amgen and Sonofi, Project with Amgen. Prof. Christof Rader: nothing. Dr. med. Stephan Reppenhagen: nothing. Prof. Ulrich Smolenski: Reports and fees from several companies. Prof. Markus Tingart: nothing. Prof. Ina Kopp: nothing. Dozent Ivan Sirotnin: nothing. Prof. Steffen J. Breusch: nothing.

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