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Table 1. Previous studies in relation to associated factors for All ONFH or non-steroidal ONFH (ONFH: osteonecrosis of the femoral head)

Study design: Comparison studies

Ref. No.	Authors/Year/Country	Study Design/Year/ Follow-up period	Subjects (M: male, F: female, A: alcohol-induced, S: steroid-induced, O: others)	Mean (or median) age (M: male, F: female)	Main result
1	Hadjigeorgiou GM, et al. 2007 Greece	Case-control 2002-2004	Case: 104 (M: 75/F: 29) Control: 113 (M: 83/F: 30) matched for age, sex	38.5 39.8	no association PONI polymorphism: M55L alleles and genotypes PONI polymorphism: Q192R O alleles (vs. R) OQ genotype (vs. OR/RR) OR (95%CI) = 2.21 (1.30 - 3.42) OR (95%CI) = 2.26 (1.29 - 4.19)
2	Hong JM, et al. 2007 Korea	Case-control 2002-2005	Case: 384 (M: 306/F: 78, 1:129/A:196/S:59) Control: 237 (M:151/F:86)	49.4 39.8	HIF1 α polymorphism: Among male idiopathic ONFH, allele frequency of -2755C>A, genotype frequency of +41224T>C and +51610C>T, and haplotype frequency of CTCC was significantly higher than controls (p=0.0409, 0.0113, 0.0269, 0.017, respectively).
3	Koo KH, et al. 2006 Korea	Case-control 2003-2005	Case: 103 (M: 87/F: 16, 1:50/S:29/A:24) Control: 103 (M: 87/F: 16) matched for age, sex	38.4 37.9	Variables eNOS: 27 bp repeat polymorphism in intron 4 [For all ON] 4a allele (vs. 4b) 4a/b genotype (vs. 4a/a+4b/b) [For idiopathic ON] 4a allele (vs. 4b) 4a/b genotype (vs. 4a/a+4b/b) eNOS: Glu288Asp polymorphism in exon 7 Frequency (cases vs. controls) 6.8% vs. 2.4%, p=0.0345 13.6% vs. 4.9%, p=0.0302 9.0% vs. 2.4%, p=0.0297 18.0% vs. 4.9%, p=0.0246 no difference
4	Björkman A, et al. 2004 Sweden	Case-control 1987-2001	Case: 63 (M: 27/F: 36, 1:35/S:23/A:5) Control: 282	-	factor V Leiden or prothrombin 20210A gene mutation [For idiopathic ON] OR (95%CI) = 2.7 (1.2 - 5.8) [For steroid/alcohol-induced ON] no association
5	Zalavras CG, et al. 2004 Greece	Case-control -	Case: 72 (M: 51/F: 21, 1:23/Secondary: 49) Control: 300 healthy blood donors	31	Variables [For all ON] factor V Leiden prothrombin 20210A gene mutation either mutation [For idiopathic ON] factor V Leiden prothrombin 20210A gene mutation either mutation [For secondary ON] factor V Leiden prothrombin 20210A gene mutation either mutation OR (95%CI) 4.5 (2.0 - 10.0) 1.6 (0.4 - 6.1) 3.6 (1.8 - 7.3) 5.7 (1.8 - 17.5) 3.5 (0.7 - 17.4) 5.5 (2.1 - 14.9) 4.0 (1.6 - 10.0) 0.8 (0.1 - 6.2) 2.8 (1.2 - 6.6)

Table continues.

Table 1. (continued)

Ref. No.	Authors/Year/Country	Study Design/Year/ Follow-up period	Subjects (M:female, F:female, A:alcohol-induced, S:steroid-induced, O:others)	Mean (or median) age (M:male, F:female)	Main result
6	Hadjiagapiou GM, et al. 2004 Greece	Case-control	Case:51 (M:35/F:16) Control:86 (M:56/F:30) matched for age, sex	36.2 31.2	While matter lesion (WML) were detected in 29 (29/51; 56.9%) patients with osteonecrosis of the femoral head ($p<0.0001$, compared to control group). The frequency of history of corticosteroid treatment was statistically lower in patients with WML compared to those without it (58.6 vs. 90.1%, $p=0.03$).
7	Sakata R, et al. 2003 Japan	Case-control 1994-2001	Case:43 (M:34/F:9) without history of systemic corticosteroid use Control:86 (M:68/F:18) matched for ethnicity, gender, age, department, date of initial examination	M:46.53 F:54.11 M:44.65 F:54.44	Variables [Among male] Occupation by workload intensity (heavier vs. lighter) BMI at examination ($/\text{kg}/\text{m}^2$) ALHD2 genotype (1/1 vs. 1/2 or 2/2) Frequency of green tea drinking (<3 or 4 times/w vs. everyday) Cumulative alcohol consumption ($/\text{drink-years}$) OR (95%CI) 5.785 (1.211 - 27.635) 0.787 (0.601 - 1.032) no association no association 1.016 (1.004 - 1.028)
8	Tektomidou MG, et al. 2003 Greece	Comparison study	30 primary APS patients (M:7/F:23) without history of corticosteroid use 19 SLE patients (M:5/F:14) without history of corticosteroid use 10 without aCL, 9 with aCL but not APS 30 healthy subjects (M:7/F:23) matched for age and sex to the patients with primary APS *APS: antiphospholipid syndrome, aCL: anticardiolipin antibodies		Prevalence of asymptomatic avascular osteonecrosis primary APS patients: 20% SLE patients: 0% healthy subjects: 0%
9	Miller KD, et al. 2002 US	Comparison study 1999	339 asymptomatic HIV-infected adults (M:311/F:28) 118 HIV-negative volunteers matched for age and sex	with ON: 44.4, without ON: 41.9	Prevalence of osteonecrosis of hip on MRI: HIV-infected 4.4%, HIV-negative 0% Among HIV-infected patients, osteonecrosis occurred more frequently in those with: any lifetime use of systemic corticosteroids, lipid lowering agents, or testosterone a history of routine exercise by weightlifting or bodybuilding detectable levels of anticardiolipin antibodies
10	Miyamishi K, et al. 1999 Japan	Case-control 1996-1997	Case:50 (M:34/F:16, S:20/A:18/E:12) Control: A. 50 healthy Japanese volunteers (M:34/F:16) B. 9 traumatic ON patients (M:5/F:4) C. 23 osteoarthritis (OA) patients (M:7/F:16)	44.4 44.4 30.3 45.7	Case vs. Control A: high apo B/apo A1 ratio was significantly associated The apo B/apo A1 ratio in the cases was significantly higher than that in the control A ($p<0.001$), control B ($p<0.01$), or control C ($p<0.001$), but there was no significant difference between the three control groups.

Table continues.

Table 1. (continued)

Ref. No.	Authors/Year/Country	Study Design/Year/ Follow-up period	Subjects (M: male, F: female, I: idiopathic, A: alcohol-induced, S: steroid-induced, O: others)	Mean (or median) age (M: male, F: female)	Main result
11	Konopliakas AV, et al. 1997 US	Case-control	Case: 40 (M: 25/F: 15, S: 21/A: 9/I: 7/O: 3) Control: 100 (M: 52/F: 48) from healthy laboratory personnel	34.3 37	Presence of antinuclear antibody titer: Case 37.5%, Control 1% (p<0.001) Among cases: positive for IgM alone: 15% positive for IgA alone: 15% positive for IgM and IgA: 7.5%
12	Moskai JT, et al. 1997 US	Comparison study 1987-1995	Case: 19 (M: 5/F: 14), idiopathic	52	16 patients had an elevated serum cholesterol level (220+ mg/dl). The patients with idiopathic avascular osteonecrosis had statistically significantly (p<0.0031) elevated cholesterol levels compared with the value expected for the general population.
13	Shibata A, et al. 1996 Japan	Case-control 1988-1994	Case: 90 (M: 64/F: 26) without history of systemic corticosteroid use Control: 180 (M: 128/F: 52) matched for sex, age, ethnicity, department	M: 49.0, F: 56.7 M: 49.0 F: 56.3	<p>Variables [Among male]</p> <p>Smoking habit (ex-smoker, current vs. non-smoker) no association</p> <p>Daily no. of cigarettes (1-9, 10-19, 20+ vs. non- or ex-smoker) no association</p> <p>Pack-years (<10, <20, 30+ vs. never) no association</p> <p>Drinking habit (current vs. non-drinker or ex-drinker) 27.09 (2.80 - 262.35)</p> <p>Daily alcohol consumption [ml] (<56, 56-84, 84+ vs. non-drinker or <28) 10.23 (1.02 - 102.12), 17.64 (2.74 - 113.73), 36.71 (5.51 - 244.74) trend p<0.001</p> <p>Cumulative alcohol consumption [drink-years] (<20, 20-30, 30+ vs. non-drinker or <10) 1.61 (0.16 - 16.27), 6.92 (0.48 - 99.18), 45.94 (5.64 - 374.26) trend p<0.001</p> <p>Flushing pattern no association</p> <p>History of liver diseases 4.79 (0.93 - 24.65)</p> <p>Occupational history no association</p> <p>BMI (<23, 23+ vs. <23) 0.16 (0.04 - 0.67), 0.16 (0.04 - 0.62), trend p<0.05</p>

Table continues.

Table 1. (continued)

Ref. No.	Authors/Year/Country	Study Design/Year/ Follow-up period	Subjects (M: male, F: female, Idiopathic, A: alcohol-induced, S: steroid-induced, O: others)	Mean (or median) age (M: male, F: female)	Main result
14	Hirota Y, et al 1993 Japan	Case-control 1988-1990	Case: 118 (M: 83, F: 35) without history of systemic corticosteroid use Control: 236 (M: 166, F: 70) matched for sex, age, ethnicity, department, date of initial examination	48.4 48.3	Variables Alcohol drinking (former, occasional, regular vs. never) 1.0 (0.2 - 6.2), 3.2 (1.1 - 9.2), 13.1 (4.1 - 42.5), trend p<0.001 Weekly ethanol intake [g/week] (<320, 320-799, 800+ vs. nondrinker) 2.8 (1.0 - 7.8), 9.4 (3.0 - 29.0), 14.8 (3.8 - 57.2), trend p<0.001 Drink-years (<3200, 3200-7999, 8,000+ vs. never) 2.2 (0.7 - 6.9), 9.7 (2.6 - 36.1), 12.9 (3.8 - 43.4), trend p<0.001 Cigarette smoking (former, current vs. never) 3.3 (0.9 - 11.6), 4.7 (1.5 - 14.5), trend p<0.01 Daily no. of cigarettes smoked (<20, 20+ vs. nonsmoker) 1.7 (0.6 - 4.5), 2.6 (1.1 - 6.0), trend p<0.05 Pack-years (<10, 10-19, 20+ vs. never) 1.6 (0.4 - 6.3), 6.6 (1.7 - 25.7), 6.5 (1.9 - 21.9), trend p<0.005 Daily occupational energy consumption [kcal/day] (1,900-2,499, 2,500+ vs. <1,900) 1.0 (0.4 - 2.4), 2.0 (0.9 - 4.6), trend p<0.05 Body mass index [kg/m ²] (25+ vs. <25) no association History of liver dysfunction 2.2 (1.0 - 5.2)
15	Naumann T, et al 1990	Comparison study 1982-1987 mean: 2 years 11 months	Lorenz group: 77 patients with 92 congenital dislocation of the hip joint, reduced with a Hoffman-Daimler brace and subsequently placed in a spica cast in Lange position after a period in the Lorenz position (M: 8, F: 69) Fettweis group: 43 patients with 48 congenital dislocation of the hip joint, reduced the same way but retained in a spica (M: 4, F: 39)	8 months 2 weeks 6 months	The Lorenz group showed 10 (out of 92, 10.9%) grade II and III femoral head necrosis, whereas there was only one (out of 48, 2.1%) grade III osteonecrosis in the Fettweis group.

Table continues.

Table 1. (continued)

Ref. No.	Authors/Year/Country	Study Design/Year/ Follow-up period	Subjects (M: male, F: female, O: others) A: alcohol-induced, S: steroid-induced, O: others	Mean (or median) age (M: male, F: female)	Main result																				
16	Matsuo K, et al 1988 Japan	Case-control 1980-1985	Case: 112 (M: 94/F: 18) without history of systemic corticosteroid use Control: 168 (M: 140/F: 28) matched for sex, age, ethnicity, hospital, date of initial diagnosis	43 43	OR (95%CI or p value) Alcohol drinking (former, occasional, regular vs. never) 4.0 (0.6 - 26.0), 5.1 (1.4 - 17.5), 7.8 (2.6 - 23.6) Weekly alcohol consumption [ml/week] (<400, 400-1000, 1,000+ vs. nondrinker) 3.3 (1.2 - 8.7), 9.8 (3.2 - 30.6), 17.9 (3.4 - 95.4), trend p<0.001 Cigarette smoking (former, current vs. never) 1.3 (0.4 - 4.6), 3.9 (1.3 - 11.7) Daily no. of cigarettes smoked (<20, 20+ vs. nonsmoker) 3.0 (p<0.05), 3.0 (p<0.05) Daily occupational energy consumption no association Obesity no association History of liver dysfunction 5.2 (2.4 - 11.2)																				
17	Powell EN, et al 1986 US	Comparison study 1966-1983	36 children with 49 complete dislocations (M: 5/F: 31)		Correlation of surgery type versus avascular necrosis																				
<table border="1"> <thead> <tr> <th>Type</th> <th>Partial avascular necrosis (%)</th> <th>Total avascular necrosis (%)</th> <th>Additional surgery (%)</th> <th>Age (mo)</th> </tr> </thead> <tbody> <tr> <td>Open reduction alone</td> <td>4/16 (25)</td> <td>0/16 (0)</td> <td>6/16 (0)</td> <td>16</td> </tr> <tr> <td>Open reduction/VDO</td> <td>4/18 (22)</td> <td>1/18 (5.5)</td> <td>1/18 (61.1)</td> <td>27</td> </tr> <tr> <td>Open reduction/incomplete</td> <td>7/15 (46.7)</td> <td>0/15 (0)</td> <td>10/15 (66.7)</td> <td>29</td> </tr> </tbody> </table>						Type	Partial avascular necrosis (%)	Total avascular necrosis (%)	Additional surgery (%)	Age (mo)	Open reduction alone	4/16 (25)	0/16 (0)	6/16 (0)	16	Open reduction/VDO	4/18 (22)	1/18 (5.5)	1/18 (61.1)	27	Open reduction/incomplete	7/15 (46.7)	0/15 (0)	10/15 (66.7)	29
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Table 2. Previous studies in relation to associated factors for All ONFH or non-steroidal ONFH (ONFH: osteonecrosis of the femoral head)

Study design: Observational studies without comparison group, Descriptive studies, or Case series

Ref. No.	Authors/Year/Country	Study Design/Study year/follow-up period	Subjects (M:male, F:female, I:idiopathic, A:alcohol-induced, S:steroid-induced, O:others)	Mean (or median) age (M:male, F:female)	Main result
18	Stieb-Furno S, et al 2007 France	observational study - 2 years	4,500 pregnancies	-	3 patients (4 hips) of pregnancy-related hip disease were observed (1 case of transient osteoporosis of the hip and 2 cases of occult fracture of the femoral head). There were 6 patients (9 hips) with transient osteoporosis of the hip, 4 patients (6 hips) with occult fracture of the femoral head, 1 patient with osteonecrosis of the femoral head, and 1 coxitis in a patients with ankylosing spondylitis.
19	Morse CG, et al 2007 US	observational study 1999-2002 median: 23 months	12 women with definite gestational or early postpartum hip disease (including the 3 cases of the 2-year observational study)	43	On the basis of the follow-up MRI, 3 patients (1.3%) received a diagnosis of osteonecrosis of the femoral head (bilateral for all patients), for an incidence of 0.65 cases per 100 person-years (95%CI, 0.13-1.89 cases per 100 person-years).
20	Balzer S, et al 2006 Germany	observational study 1993-2004 15 months	239 asymptomatic HIV-infected adults	16.1	Seven out of these 72 patients developed avascular osteonecrosis of the femoral head.
21	Xie L, et al 2005 China	observational study 2003-2004 12 months	72 children and adolescents with locoregional pelvic malignancies, receiving regional deep hyperthermia (RHT) with systemic chemotherapy without steroid. Twenty of the patients received subsequent pelvic irradiation. (M:24/F:48)	38.2	Some patients who complained of joint pain were given MRI examinations of their femoral head. Of the individuals receiving MRI examination in the 12 month duration of the study, 23.1% (18 of 78 patients) showed signs of femoral head necrosis.
22	Yamada N, et al 2003 Japan	observational study - at least two years	383 clinically diagnosed SARS patients (M:160/F:223)	11.5 months	Of the 55 children, 27 (31 dislocation) were followed up until they were over six years of age. Only one had radiological evidence of avascular necrosis of the femoral head.
23	Agus H, et al 2002 Italy	observational study 1993- average: 44.5 months	54 infant (67 dysplastic hips) treated by the same surgical technique, including iliopectus and adductor (M:5/F:49)	11.9 months	The cumulative incidence of overall avascular necrosis was 27% and that of severe avascular necrosis was 7%.

Table continues.

Table 2. (continued)

Ref. No.	Authors/Year/Country	Study Design/Study year/follow-up period	Subjects (M:male, F:female, I:idiopathic, A:alcohol-induced, S:steroid-induced, O:others)	Mean (or median) age (M:male, F:female)	Main result
24	Dzik-Jurasz AS, et al 2001 UK	observational study - mean time of MRI scanning after the end of treatment: 33.7 months	34 patients previously treated for anal cancer by chemoradiation, currently disease free (M:11/F:23)	66.7	No cases (0/34) of symptomatic or asymptomatic femoral head osteonecrosis were detected.
25	Bonfanti P, et al 2001 Italy	observational study 1997- average: 10.7 months	1,207 HIV-infected patients with protease inhibitors (M:880/F:327)	37.1	During treatment with protease inhibitors, 4 cases of bilateral osteonecrosis of the femoral head have been reported out of 1,073 person-years.
26	Boechat MI, et al 2001 US	observational study 1990-1996 mean: 3 years	205 children with chronic renal failure but not end stage (M:159/F:46)	6	Radiographic findings of avascular necrosis (AVN) of the femoral head were seen in 14 of 205 patients (7%). The frequency of AVN was similar in boys and girls, and was not related to the duration of renal disease, type of renal disease, or growth hormone therapy. In two instances, AVN developed while the patients were receiving corticosteroids before entering this study.
27	Winqvist EW, et al 2001 US	observational study 1950-1995	107 men with testicular cancer receiving chemotherapy with curative intent and with a minimum 2 years of follow-up	-	occurrence of ONFH: 2% (2/107) duration from initiation of chemotherapy to diagnosis: 45 and 47 months total equivalent prednisone dose during chemotherapy: 2,820 mg and 2,40mg
28	Williams PR, et al 1999 UK	observational study 1987- a minimum of 9 years	83 infants (117 type III-IV hips) using Aberdeen splint due to a 'high risk' for developmental dysplasia of the hip	-	incidence of avascular necrosis: none
29	Enrici RM, et al 1998 Italy	observational study 1972-1996 average: 78 months	784 patients treated for Hodgkin's disease either with chemotherapy (CT) containing steroids, combined in some cases with subdiaphragmatic radiotherapy (RT), or with subdiaphragmatic RT combined with CT (M:431/F:353)	30.5	9 cases of avascular osteonecrosis emerged in the head of the femur, appearing between 23 and 97 months after initial treatment. All the patients in whom avascular osteonecrosis appeared had received, either as initial treatment or after relapse, RT/CT or CT including steroids.
30	Thomas IH, et al 1989 Australia	observational study 1970-1980	72 infants and children with 87 dislocated hips treated by open reduction (M:33/F:59)	22 months	Avascular necrosis (AVN) was observed in 37% of the hips, yet open reduction did not appear to contribute to the development of AVN as its prevalence was similar in hips treated by open or closed reduction in our institution.
31	Gregosiewicz A, et al 1988 Poland	observational study -	1,211 hips with congenital dislocation	-	Avascular osteonecrosis was detected in 254 (21%) of all hips.

Table continues.

Table 2. (continued)

Ref. No.	Authors/Year/Country	Study Design/Study year/follow-up period	Subjects (M:female, F:female, Induced, Idiopathic, Alcohol-induced, Steroid-induced, Others)	Mean (or median) age (M:female, F:female)	Main result
32	Hajajainen J, et al 1985 Finland	observational study 1966-1981	546 renal transplant patients (639 transplants) with graft survival for a minimum of 12 months. Glucocorticosteroids and azathioprine were used as immunosuppressive agents. (M:312:F:234)	38	Aseptic hip necrosis developed in 39 hips in 29 patients (5.3%) from 3 to 121 months (mean 22 months) after the renal transplantation.
33	Zabinski SJ, et al 1998 US	descriptive study	545 primary total hip arthroplasties performed in 507 patients with RA (M:40:F:467)	56.1	Osteonecrosis was identified in 66 specimens (12.1%) in one of 2 discrete forms. 32 specimens (5.9%) contained classic subchondral avascular necrosis. 34 specimens (6.2%) contained osteonecrosis in association with degenerative changes. Corticosteroid therapy was used in 81% of patients with avascular necrosis and 68% with degenerative osteonecrosis. This was significantly greater prevalence than in patients without osteonecrosis (23%). Average daily prednisone dosage was 8 mg.
34	Hamil I, et al 1993 US	descriptive study 1974-1991	5,278 patients treated for cancer at a major pediatric oncology center	-	Avascular femoral head osteonecrosis was identified in 15 patients. Both steroids and radiation therapy appear implicated in the pathogenesis of the avascular osteonecrosis: nine patients received high cumulative doses of prednisone (3.4-14 g/m ²), four had received 35-64.8 Gy local irradiation involving the femoral head, and one underwent total body irradiation (1.2Gy).
35	Ries MD, et al 2002 US	case series 1992-1998	38 patients (M:24:F:14)	37.4	7 patients were HIV positive, and 31 were HIV negative. Of the 7 patients who were HIV positive, 4 (57%) had none of the known risk factors for osteonecrosis.
36	Castro FP Jr and Harris MB 1999 US	case series 1984-1998	172 patients (M:122:F:50) with 245 hips	44	Distribution of Patients and Hips by Causes, Steinberg Stage

	Steroid	Alcohol	Idiopathic	Total
Patients (hips)	69 (103)	63 (88)	40 (54)	172 (245)
Male	32	61	29	122
Female	37	2	11	50
Age (SE)	39 (2)	49 (1)	42 (2)	44 (1)
Steinberg stage (patients [hips])				
I	6 (10)	2 (2)	5 (6)	13 (18)
II	20 (29)	4 (6)	13 (18)	37 (53)
III	19 (25)	12 (15)	22 (30)	53 (70)
IV-V	24 (39)	45 (65)	0 (0)	69 (104)

Table continues.

Table 2. (continued)

Ref. No.	Authors/Year/Country	Study Design/Study year/follow-up period	Subjects (M:male, F:female, I:idiopathic, A:alcohol-induced, S:steroid-induced, O:others)	Mean (or median) age (M:male, F:female)	Main result
37	Collaborative Osteonecrosis Group 1999 US	case series 1980-1996	101 patients with multifocal osteonecrosis (defined as disease involving three or more separate anatomic sites) (M:26/F:75)	36	Ninety-two of the 101 (91%) patients had a history of corticosteroid therapy. Twenty (20%) patients had a history of smoking at least one pack per day of tobacco or had a greater than 10 pack year smoking history. Ten (10%) patients consumed more than 400ml. per week of alcohol. Twelve patients (of 14 tested) were found to have a coagulation disorder. All 101 patients had femoral head involvement. Bilaterality was common (98%).
38	Montella BI, et al 1999 US	case series	13 pregnant women	31.5	Eleven of the thirteen women were primigravids, and the patients typically first had the pain late in the second or third trimester of pregnancy. The women tended to have a small body frame and a relatively large weight gain during the pregnancy.
39	LaPorte DM, et al 1998 US	case series 1976-1996	32 patients with multifocal osteonecrosis (defined as involvement of 3 separate anatomic sites) (M:8/F:24)	34	Associated factors included systemic lupus erythematosus (13 patients), inflammatory bowel disease (5 patients), malignancy (4 patients), and renal transplantation (3 patients). Thirty of the 32 patients (94%) had a history of corticosteroid therapy, with the other 2 patients found to have a coagulopathy. All 32 patients had bilateral femoral head involvement.

Table 3. Previous studies in relation to associated factors for All ONFH or non-steroidal ONFH (ONFH; osteonecrosis of the femoral head)

Study design: Case report

Ref. No.	Authors/Year/ Country	number of reported cases	underlying disease or condition	case ID	sex (M: male, F: female)	age at diagnosis with underlying disease	age at diagnosis with ONFH	site of ONFH	status of other risk factors for ONFH
40	Lima GA, et al. 2005 Brazil	2	AIDS	Case 1 Case 2	F F	43 41	52 43	left left	none mestrol acetate use (synthetic progestational steroid), 800mg/day for wasting syndrome systemic corticosteroid use for eight months due to a neurological condition
41	Lien YH, et al 2005 US	1	Fabry disease	M	M	8	32	bilateral	none
42	Rollot F, et al 2005 France	3	Hemochromatosis with homozygous for the C282Y mutation on HFE gene	Case 1 Case 2 Case 3	M F M	55 37 46	46 46 46	bilateral bilateral right	none none none
43	Siddiqui SA, et al 2004 US	4	HIV infection	Case 1 Case 2 Case 3 Case 4	M F M M	30 23 36 39	34 33 47 39	bilateral bilateral bilateral bilateral	none none "social drinker" taking 1 to 2 drinks daily cigarettes: 1 pack daily; alcohol: 1 to 2 drinks daily
44	Kisielinski K, et al 2004 Germany	1	daily inhaled glucocorticoid therapy for chronic bronchitis	F	F	49	69	left	At aged 54, she had had an intracapsular fracture of the femoral neck that had been treated immediately by screw-plate fixation. The fixation device was left in place and the femoral head remained viable. She experienced no hip pain until the onset of the current episode.
45	Smida M, et al 2003 Tunisia	2	GH (growth hormone) deficiency treated by GH	Case 1 Case 2	M M	12 11	15 17	left right	none none
46	Orpen N, et al 2003 England	3	surgery for lumbar spinal stenosis under prolonged hypotensive anaesthesia in the prone position	Case 1 Case 2 Case 3	F F M	68 72 73	68 (4 month after surgery) 73 (5 month after surgery) 73 (6 month after surgery)	bilateral bilateral left	none none none

Table continues.

Table 3. (continued)

Ref. No.	Authors/Year/ Country	number of reported cases	underlying disease or condition	case ID	sex (M: male, F: female)	age at diagnosis with underlying disease	age at diagnosis with ONFH	site of ONFH	status of other risk factors for ONFH
47	Bojko P, et al 2003 Germany	3	relapsed ovarian cancer receiving high-dose chemotherapy with excessive single-dose treosulfan followed by autologous peripheral blood stem cell transplantation	Case 1 Case 2 Case 3	F F F	49 40 39	53 47 43	bilateral right bilateral	none none none
48	Aguiar De Aragão P, et al 2002 Brazil	1	hyperlipidemia in AIDS with protease inhibitors		M	7	10 (7 month after the plasma triglyceride levels reached 460 mg/dl)	bilateral	none
49	Kubo T, et al 2000 Japan	1	congenital antithrombin III deficiency		M	34	35	bilateral	none
50	Koller E, et al 2000 US	3	HIV seropositive patients receiving megestrol acetate	Case 1 Case 2 Case 3	M M M	- - -	55 36 34	bilateral unilateral bilateral	none undisclosed dose and duration of corticosteroids concurrent with pentamidine administration none
51	Caniggia M, et al 1994 Italy	2	pregnancy	Case 1 Case 2	F F	- -	26 (at the end of the seventh month of her first pregnancy) 36 (during the last weeks of uncomplicated second pregnancy)	left left	taking oral contraceptives for four years discontinuing the treatment five months prior to conception taking oral contraceptives intermittently in the previous eight years discontinuing contraceptives four months before conception

Table 4. Previous studies in relation to associated factors for steroid ONFH (ONFH: osteonecrosis of the femoral head)

Study design: Comparison studies

Ref. No.	Authors/Year/Country	Study Design/Year/ Follow-up period	Subjects (M: male, F: female)	Mean (or median) age	Main result
52	Hirata, et al 2007 Japan	Case-control 1983-2004	Case: 34 (M: 22/F: 12) following renal transplantation and steroid use Control: 124 (M: 91/F: 33) following renal transplantation and steroid use	39.5 35.0	Variables apolipoprotein B (C7623T) CT TT (vs CC) apolipoprotein B (G12619A) GA AA (vs GG) apolipoprotein AI (G-75A) GA AA (vs GG) apolipoprotein AI (C83T) CT TT (vs CC) OR (95%CI) 6.37 (1.53 - 26.5) 0.55 (0.06 - 5.11) 1.41 (0.57 - 3.50) 1.39 (0.39 - 5.05)
					Variables HDL LDL LDL/HDL ratio P value 0.161 0.470 0.227
53	Hediri, et al 2007 Tunisia	Case-control 1986-2004	Case: 15 (M: 11/F: 4) following renal transplantation and steroid use Control: 15 following renal transplantation and steroid use matched for age, gender, date of renal transplantation	40.8 38.3	Variables Duration of dialysis (year) Mean rate of acute rejection episodes Cumulative mean dose of glucocorticoid Weight gain at 1 year after RT Serum creatinine P value NS 0.058 0.04 NS NS
54	Hirata, et al 2007 Japan	Case-control 1983-2004	Case: 20 (gender ratio: unknown) following renal transplantation Control: 92 (gender ratio: unknown) following renal transplantation (unmatched)	unknown unknown	Variables Molecular weight phenotype of apolipoprotein A LMW (vs HMW) OR (95%CI) 5.75 (1.76 - 18.74)
55	Kaneshiro, et al 2006 Japan	Case-control 2002-2006	Case: 26 (M: 53.8%) Control: 75 (M: 42.6%) unmatched	44.5±13.7 43.4±14.7	Variables Mifedoniam clearance <=9.5mL.kg ⁻¹ .min ⁻¹ (vs >9.5mL.kg ⁻¹ .min ⁻¹) OR (95%CI) 9.08 (2.79 - 29.6)

Table 4 continues

Table 4. (continued)

Ref. No.	Authors/Year/Country	Study Design/Year/ Follow-up period	Subjects (M:male, F:female)	Mean (or median) age	Main result
56	Talano, et al 2005 US	Case-control 1998-	Case: 49 (M:38/F:11) with myeloma and dexamethasone treatment Control: 504 (M:290/F:214) unmatched	52.0 (SD:8.6) 58.0 (SD:9.85)	Variables Younger age Female Larger steroid dose unit/40mg OR (95%CI) 0.962 (0.934 - 0.991) 0.392 (0.196 - 0.785) 1.028 (1.013 - 1.044)
57	Nagasawa, et al 2006 Japan	Case-control 1993-1998	60 newly diagnosed SLE patients requiring steroid therapy Warfarin (+) group: 31 (M:2/F:29) Warfarin (-) group: 29 (M:3/F:26) ↓ Case: 18 (M:4/F:14) Non-case: 42 (M:1/F:41)	30.2 (13 - 56) 29.8 (15 - 50) 30.8 29.7	Variables Male Steroid pulse therapy CNS disease P value <0.05 <0.001 <0.05
58	Nagasawa, et al 2005 Japan	Case-control 1994-1997 (>5yrs Follow-up)	Case: 15 (M:2/F:13) with SLE and high dose steroid therapy Control: 30 (F:30) with SLE and high dose steroid therapy	29.1 31.1	Variables Steroid pulse therapy (+) Total cholesterol ↑ WBC ↑ Albumin ↓ P value <0.05 <0.05 <0.05 <0.05
59	Asano, et al 2004 Japan	Case-control 1970-	Case: 31 (M:20/F:11) after renal transplantation Control: 106 (M:79/F:27) after renal transplantation unmatched	38.6 36.5	Variables PAL-1 genotype 4G/5G (vs 5G/5G) 4G/4G (vs 5G/5G) MTHFR genotype CT (vs CC) TT (vs CC) OR (95%CI) 0.65 (0.17 - 2.47) 1.81 (0.48 - 6.78) 0.52 (0.20 - 1.39) 0.96 (0.30 - 3.08)
60	Inoue, et al 2003 Japan	Case-control 1983-1992	Case: 18 (M:11/F:7) after renal transplantation Control: 72 (M:51/F:21) after renal transplantation matched for age and gender	33.8 (20.4-56.2) 32.8 (19.0-61.2)	Variables BUN ≥= two-fold rise Steroid daily dosage ≥= 25.0mg OR (95%CI) 2.17 (0.67 - 7.03) 7.06 (0.36 - 13.8)

Table 4 continues

Table 4. (continued)

Ref. No.	Authors/Year/Country	Study Design/Year/ Follow-up period	Subjects (M: male, F: female)	Mean (or median) age	Main result	P value
61	Sakai, et al 2003 Japan	Cohort -	Cyclosporin A: 32 (M:21/F:11) Tacrolimus: 32 (M:21/F:11) matched for age, gender, and renal allograft	35.1±9.4 35.3±10.1	Osteonecrosis: 5 Osteonecrosis: 0	0.026
62	Asano, et al 2003 Japan	Case-control 1970-	Case: 30 (M:20/F:10) after renal transplantation Control: 106 (M:78/F:28) after renal transplantation	40.5 (25-63) 36.2 (9-62)	Variables ABCBI genotype 3435TT (vs 3435CC or CT) 2677(TorA)(TorA) (vs 2677GG or G(TorA))	OR (95%CI) 0.10 (0.01 - 0.84) 0.30 (0.09 - 0.98)
63	Asano, et al 2003 Japan	Case-control 1970-	Case: 26 (gender ratio: unknown) after renal transplantation Control: 54 (gender ratio: unknown) after renal transplantation unmatched	unknown unknown	Variables CYP2D6 IM (vs EM) CYP2C19 PM (vs EM)	OR (95%CI) 1.8 (0.4 - 7.9) 1.0 (0.2 - 6.8)
64	Torii, et al 2001 Japan	Case-control 1981-1998	Case: 19 (M:10/F:9) after bone marrow transplantation Control: 81 (M:45/F:36) after bone marrow transplantation	28.6±7.85 34.2±10.4	Variables Age (10 years increment) Chronic GVHD (Yes/No) Pulse regimen (Yes/No)	OR (95%CI) 0.47 (0.234 - 0.934) 5.57 (1.032 - 30.1) 11.3 (3.15 - 40.44)
65	Lausten, et al 1998 Denmark	Cohort 1968-1995	High-dose steroid: 374 (M:206/F:168) Low-dose steroid: 376 (M:239/F:137) after a kidney transplantation	43 (6-66) 48 (7-76)	11.2% (42/374, average of 26.2 months after transplantation) 5.1% (19/376, average of 20.5 months after transplantation) P=0.002	
66	Aranow, et al 1997 US	Case-control -	66 patients with SLE and steroid treatment (M:5/F:61) Case: 8 Control: 58	34.9 (18-67)	Variables African-American origin Prednisone (>30mg/day) Migraine headache Raynaud's phenomenon	OR (95%CI) 11.5 (7.3 - 18.0) 4.2 (2.5 - 6.9) 3.5 (2.2 - 5.4) 1.8 (1.1 - 2.8)

Table 4 continues

Table 4. (continued)

Ref. No.	Authors/Year/Country	Study Design/Year/ Follow-up period	Subjects (M: male, F: female)	Mean (or median) age	Main result	P value
67	Saisu, et al 1996 Japan	Case-control 1974-1994	Case: 22 (M:17/F:5) after renal transplantations Control: 47 (M:33/F:14) after renal transplantations	31.0 (SD=8.7) 29.8 (SD=7.7)	Variables Intravenous pulse dose of methylprednisolone Maintenance dose of prednisolone	0.0009 0.0012
			After 1982 (after introduce of cyclosporin A) Case: 12 after renal transplantations Control: 44 after renal transplantations	- -	Variables Intravenous pulse dose of methylprednisolone Maintenance dose of prednisolone	0.0013 NS
68	Laustsen, et al 1988 Denmark	Cohort Case-control 1968-1987	Patients with renal transplantations Prednisone+Azathioprine: 374 (M:206) Cyclosporin/A+reduced steroid: 124 (M:69)	- -	ONFH 42/374 ONFH 4/124 (P<0.01)	
			Case: 46 Control: 46 matched for age, sex, number of transplantation, f/u time		Variables Patients with rejection (ION+: 22, ION-:35)	P value <0.05

Table 5. Previous studies in relation to associated factors for steroidal ONFH (ONFH: osteonecrosis of the femoral head)

Study design: *Observational studies without comparison group, Descriptive studies, or Case series*

Ref. No.	Authors/Year/Country	Study Design/Study year/follow-up period	Subjects (M:male, F:female)	Mean (or median) age	Main result
69	Wang, et al 2005 China	Retrospective review 1994-2001	Case: 4 (M:1/F:3)	26 (21-31)	Time to onset from steroid therapy: mean 14.5 months (4-27 months) steroid dose: mean 102mg (59-150 mg) steroid duration: mean 20 days (15-27 days)
70	Horiuchi, et al 2004 Japan	Surveillance 1990-2001			ONFH after liver transplantation has not been a clinical problem for study patients.
71	Manston, et al 2002 US	Cohort (one arm) 1997-2000	52 (M:29/F:23) after a solid organ transplantation	43 (24-65)	Prevalence: 20% one year after transplantation <40 year-old is a risk (p=0.011)
72	Koo, et al 2002 South Korea, US	Case series 1993-1997	Case: 22 (M:8/F:14)	33 (17-60)	Twenty-one of 22 patients were diagnosed within 12 months of the initiation of steroid treatment.
73	Pritchett 2001 US	Cohort (one arm)	284 (M:153/F:131) with stain during steroid exposure	51 (27-71)	Three patient (1%) developed osteonecrosis after an average of 7.5 years follow-up. Statins may offer some protection against having osteonecrosis develop when steroid treatment is necessary.
74	Bizot, et al 1998 France	Case series 1980-1997	Case: 35 (M:19/F:16) after bone marrow transplantation	26 (14-45)	Recommendation of primary total hip arthroplasty after failure of the demical treatment, according to the result from survival curve.
75	Kubo, et al 1998 Japan	Prospective study	45 subjects (M:30/F:15) after renal transplantation	33.5 (18-62)	26.7% (12/45, average 4.5 months after transplantation) Large dose steroid in pulse therapy might relate to the occurrence of ONFH.

Table 5 continues