The Journal of Arthroplasty Vol. 26 No. 7 2011

Ten-Year Follow-Up of Avascular Necrosis of Femoral Head Treated With Alendronate for 3 Years

Sanjay Agarwala, MS (Orth), MCh (Orth),* and Satyajit B. Shah, MS (Orth)†

Abstract: Although all the recent reports of the use of bisphosphonates in avascular necrosis of femoral head (AVNFH) have been encouraging, none has studied long-term effects of this novel therapy. We therefore performed a 10-year follow-up study of 40 patients (53 hips) of AVNFH treated with 3-year-long oral alendronate therapy. Rates of clinical failure defined as need for further surgical intervention, of radiologic progression for the Ficat-Arlet scale, and of collapse of femoral head showed marked reduction even at 10 years as compared to the historical data available for natural history of hips with untreated AVNFH. Alendronate given for 3 years maintains its beneficial effects for as long as 10 years and hence is a worthwhile option to postpone the need for arthroplasty in these young and active patients. **Keywords:** bisphosphonates, avascular necrosis of hip, arthroplasty.

Optimal treatment of avascular necrosis of hip (avascular necrosis of femoral head [AVNFH]) in its various stages, even today, remains controversial. The young age of these patients and variability of results of operative interventions have prompted researchers to look for some form of nonoperative therapy for this debilitating condition. Agarwala et al [1], in a prospective trial about a decade ago, were the first ones to report successful use of bisphosphonates in AVNFH to improve clinical status, retard the progression of disease, and avoid an arthroplasty. Several studies [2-6], subsequently, have confirmed effectiveness of this new therapy, but all had a limitation of a short-term follow-up not exceeding 4 years and were unanimous in recommending evaluation of this novel treatment modality for a longer term period. In this manuscript, we present our 10-year experience with a cohort of 40 patients (53 hips) who received alendronate for AVNFH in the first 3 years as a part of prospective trial initiated then. There has been no report of such a long-term follow-up of this new therapeutic approach to AVNFH.

*From the *P.D. Hinduja National Hospital and Medical Research Centre, Mahim, Mumbai, India; and †Department of Orthopedics, P.D. Hinduja National Hospital and Medical Research Centre, Mahim, Mumbai, India.*
Submitted May 21, 2010; accepted November 28, 2010.
The Conflict of Interest statement associated with this article can be found at doi:10.1016/j.arth.2010.11.010.
Reprint requests: Satyajit Shah, MS (Orth), MCh (Orth), Department of Orthopedics, P.D. Hinduja National Hospital and Medical Research Centre, Mahim, Mumbai, India.

0883-5403/2607-0027$36.00/0
doi:10.1016/j.arth.2010.11.010

Patients and Methods

From January 1998 to November 1998, we saw 64 adult patients with AVNFH. As a part of a prospective observational study approved duly by our institutional review board, alendronate treatment was considered in all but 14 who had Ficat grade 4 AVNFH with arthritic symptoms severe enough to warrant arthroplasty. Another 5 had either peptic ulcer disease or hepatorenal derangement that contraindicated the use of alendronate. Thus, 45 patients (61 hips, 16 bilateral affections) received once a day, oral, 10-mg alendronate with standard precautions that are followed with the use of any other bisphosphonate. Throughout the duration of the treatment, all patients received oral daily supplements of 500 mg of calcium and 400 IU of vitamin D_3. Analgesics were permitted as and when required and were noted in every case. In the first 3 months of treatment, all patients were advised partial weight-bearing walk using elbow or axillary crutches, and weight-bearing was increased gradually as dictated by pain tolerance. The treatment was stopped at 3 years or whenever it failed to control pain and disability, mandating a total hip arthroplasty.

Follow-up visits were scheduled every 6 weeks in the first 3 months, every 3 months until 1 year, and annually thereafter. Telephonic reminders were given to those who would not turn up for a scheduled visit. The annual visits were continued even after cessation of administration of alendronate at 3 years. At presentation and at each subsequent follow-up visit, pain and disability scores were recorded on a verbal response scale of 0 to 10 (0 for nil, 10 for maximum), whereas standing time and walking time were recorded in minutes. For bilateral hip affection, pain scores were noted for both hips, whereas

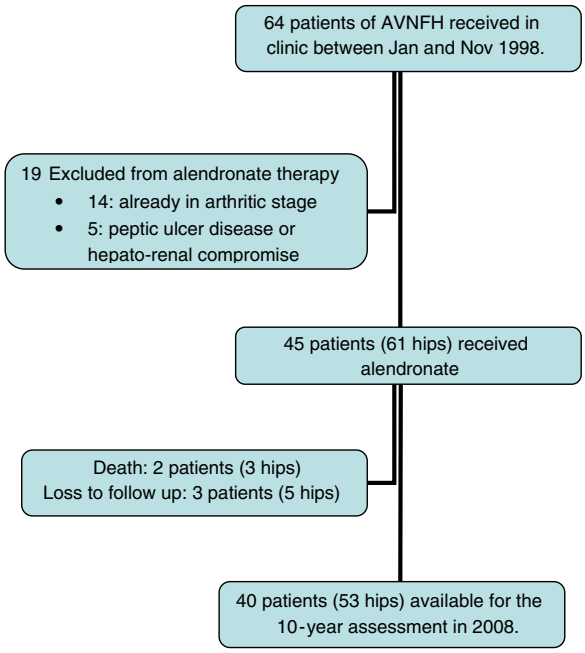

Fig. 1. Flow of patients.

other clinical parameters were recorded only for the more painful hip. The activities of daily living of Indian patients are so varied that none of the existing validated hip or lower extremity functional scoring systems could be applied, and hence, aforementioned basic clinical parameters were chosen for functional evaluation. In addition, at first visit, duration of hip pain before starting alendronate treatment was recorded, whereas at follow-up visits, analgesic consumption and side effects of the drug, if any, were noted. Discontinuation of ingestion of daily tablet for more than 2 weeks or inability to complete at least 5 months in any consecutive period of 6 months were termed as *nonadherence to treatment*. All the data recorded were compared to the corresponding parameters at previous visits and discussed openly with the patients to positively reinforce their adherence to this long-term daily treatment modality.

Plain radiograms of both hips in anteroposterior and frog lateral views were repeated at every visit. Ficat-Arlet radiographic staging of the femoral head was reported by an independent, same, blinded radiologist. Because of financial constraints, magnetic resonance imaging (MRI) study could not be performed in all the patients. It was reserved as a diagnostic tool in suspected Ficat grade 1 AVNFH.

Clinical failure was defined as the need for surgical intervention, whereas progression on plain radiograms on the Ficat-Arlet scale was termed as *radiologic failure*. Collapse rate was calculated considering the number of hips progressing to radiologic evidence of collapse (Ficat stage 3).

Initially, the study protocol was designed as a prospective observation for a period of 3 years and was duly approved by the institutional ethics committee. The present report is a retrospective assay of these 45 patients at 10 years after inclusion in the prospective trial.

Of the 45 patients (61 hips) that were started on alendronate therapy, 2 patients (3 hips) died at 2 and 5 years of treatment because of causes unrelated to the treatment or the disease, whereas 3 others (5 hips) were lost to follow-up, 1 in grade 2 as early as at 6 months because of uncontrollable pain. It was realized later that he underwent a total hip arthroplasty at some other center a couple of months later. The other 2 were 1 each in Ficat grades 2 and 3 and were lost at 5 and 6 years, respectively, because of transfer abroad. It could, however, be established through a recent e-mail communication that both did not require any further intervention to date. All others (53 hips in 40 patients) adhered well to the 3-year-long daily treatment and were available for 10-year follow-up (Fig. 1).

Median values of pain score, disability score, standing time, and walking time at various time intervals of follow-up were compared to those at baseline. Friedman test with Dunn post hoc test was used as the test of significance between groups after normality was checked by Kolmogorov-Smirnov test. Kaplan-Meier survival curves were plotted for clinical survival of the groups. Log-rank test was used as test of significance.

$P < .05$ was deemed statistically significant. SPSS 15.0 (SPSS Inc, Chicago, Ill, now IBM Corporation, New York, NY), GraphPad Instat 3 (GraphPad Software, Inc, California), and GraphPad Prism (GraphPad Software, Inc) were used to analyze the data.

Results

Mean age at presentation was 41.8 ± 9 years (range, 25-61 years); male:female sex ratio was 32:21. Ficat grade-wise distribution and duration of hip pain at presentation are mentioned in Table 1.for stage 1 and 2 hips considered together.

Clinical Survival

At 10 years, 46 (87%) of the 53 hips survived, that is, had a satisfactory clinical result. Hip loss to arthroplasty

Table 1. Ficat Stage-Wise Distribution of Hips and Duration of Hip Pain at Presentation

Ficat Stage of AVNFH at Commencement of Treatment	No. of Hips Studied	Mean Duration of Hip Pain (in mo) Before Institution of Treatment (SD) (range)	
1	15	3.1 (1.75) (1-6)	4.7 (2.81) (1-12)for stage 1 and 2 hips considered together
2	19	5.9 (2.89) (1-12)	
3	19	12.4 (7.71) (1-36)	
Total	53	7.4 (6.30) (3-36)	

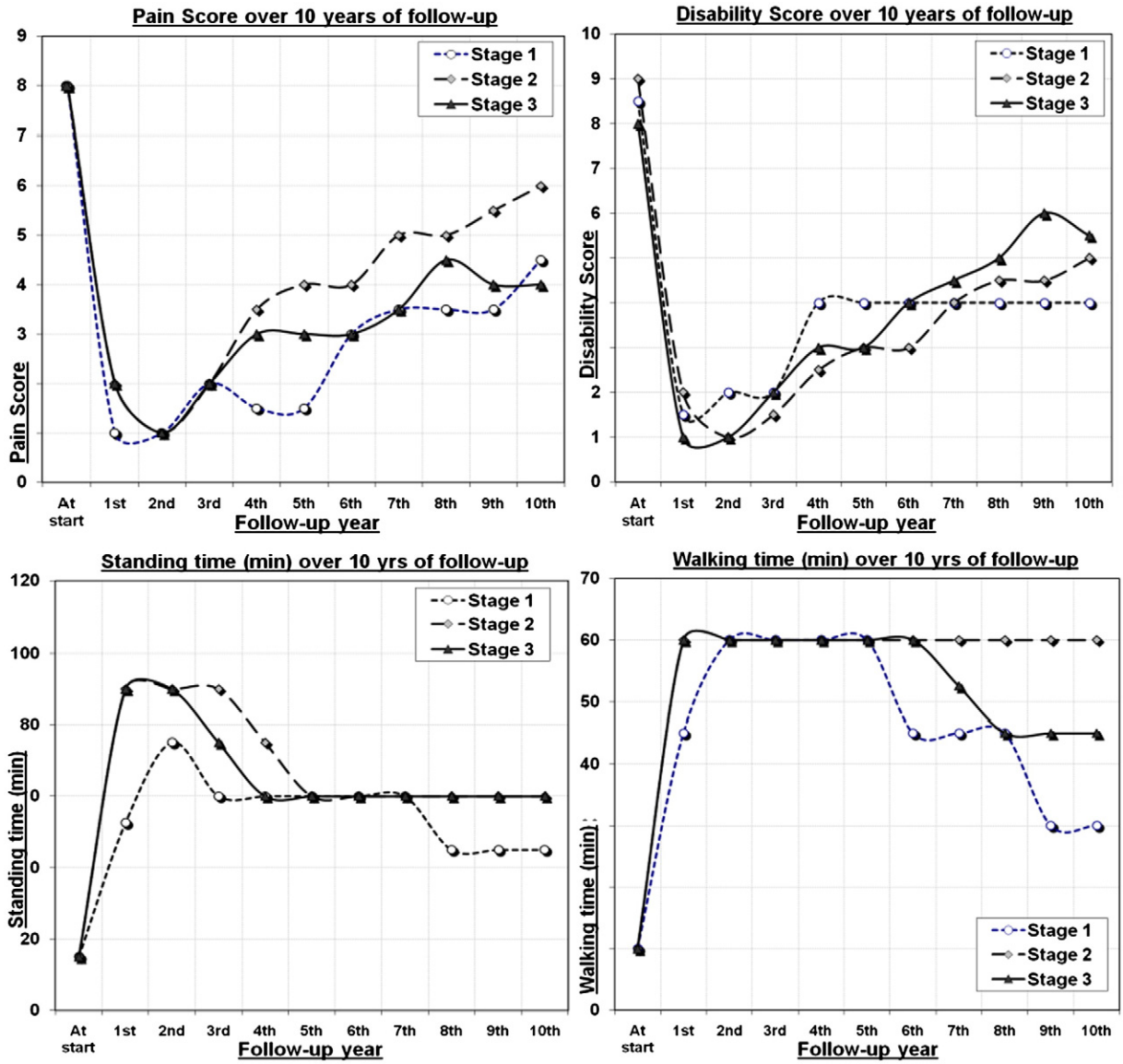

Fig. 2. The response of pain score, disability score, standing time, and walking time to treatment with alendronate.

occurred in 1 each of Ficat stage 1 (7%) and Ficat stage 2 (5%) hips and in 5 (26%) of Ficat stage 3 hips.

Fig. 2 graphically illustrates the response of pain score, disability score, standing time, and walking time to treatment with alendronate, whereas Table 2 compiles the median values of clinical parameters at various points of time.

Kaplan-Meier time survival analysis is shown in Fig. 3. Compared to Ficat stage 3 hips, stage 1 and stage 2 hips showed significantly higher survival probability (log-rank test, $P = .04$).

Radiologic Failure

Radiologic progression noted at 10-year follow-up has been shown in Table 3.

Chronological details of the 20 hips that progressed for these 10 years are shown grade wise in Fig. 4.

Collapse rate: of the 34 hips that were in precollapse stages at the onset of the study, at 10 years, 10 had collapsed, indicating a collapse rate of 29% for a period of 10 years. Mean time to collapse was 4.2 years

None of the patients during the 3 years of alendronate consumption reported any major side effect of the drug. Of the 40 patients, 7 had reported generalized muscle pain and dizziness at onset, but the symptoms were mild and self-limiting, allowing us to continue the treatment. Analgesic usage in all the patients decreased for first 2 months of onset of alendronate ingestion. All the patients adhered well to the proposed treatment schedule.

Discussion

Of all the nonoperative measures reported to halt progression of AVNFH, recent reports of use of

Table 2. Median Values of Clinical Parameters at Various Points of Time

		At Onset	At 1 Year	At 3 Years	At 7 Years	At 10 Years
	Stage 1 hips (n = 15 hips)					
Pain score	Median	8.00	1.00	2.00	3.50	4.50
	IQR	2.00	1.00	2.00	4.25	6.25
	P		.0009	.0013	.0014	.0014
Disability score	Median	8.50	1.50	2.00	4.00	4.00
	IQR	1.00	1.00	2.75	4.00	5.00
	P		.0020	.0027	.0032	.0031
Standing time	Median	15.00	52.50	60.00	60.00	45.00
	IQR	8.75	15.00	52.50	75.00	60.00
	P		.0022	.0028	.0049	.0050
Walking time	Median	10.00	45.00	60.00	45.00	30.00
	IQR	0.00	30.00	45.00	60.00	60.00
	P		.0021	.0028	.0033	.0032
	Stage 2 (n = 19 hips)					
Pain score	Median	8.00	2.00	2.00	5.00	6.00
	IQR	2.00	1.00	2.00	4.00	4.25
	P		.0001	.0002	.0003	.0011
Disability score	Median	9.00	2.00	1.50	4.00	5.00
	IQR	2.00	1.00	1.75	4.00	3.00
	P		.0013	.0021	.0021	.0028
Standing time	Median	15.00	90.00	90.00	60.00	60.00
	IQR	17.50	45.00	52.50	33.75	26.25
	P		.0015	.0021	.0022	.0022
Walking time	Median	10.00	60.00	60.00	60.00	60.00
	IQR	15.00	37.50	30.00	15.00	30.00
	P		.0015	.0022	.0022	.0022
	Stage 3 (n = 19 hips)					
Pain score	Median	8.00	2.00	2.00	3.50	4.00
	IQR	2.00	1.00	2.25	3.00	3.50
	P		.0002	.0003	.0009	.0021
Disability score	Median	8.00	1.00	2.00	4.50	5.50
	IQR	1.00	1.00	2.00	3.50	3.25
	P		.0006	.0009	.0033	.0075
Standing time	Median	15.00	90.00	75.00	60.00	60.00
	IQR	5.00	75.00	41.25	41.25	15.00
	P		.0006	.0009	.0020	.0097
Walking time	Median	10.00	60.00	60.00	52.50	45.00
	IQR	10.00	60.00	26.25	15.00	15.00
	P		.0006	.0010	.0022	.0049
	All hips together (N = 53 hips)					
Pain score	Median	8.00	2.00	8.00	2.00	8.00
	IQR	2.00	1.00	2.00	1.00	2.00
	P		3.85, E-010	1.08, E-009	6.90, E-009	4.01, E-008
Disability score	Median	8.50	1.50	2.00	4.00	5.00
	IQR	1.00	1.00	2.00	4.00	3.50
	P		2.76, E-008	7.56, E-008	3.36, E-007	1.08, E-006
Standing time	Median	15.00	60.00	75.00	60.00	60.00
	IQR	5.00	45.00	37.50	45.00	22.50
	P		3.48, E-008	8.02, E-008	3.51, E-007	1.62, E-006
Walking time	Median	10.00	10.00	10.00	10.00	10.00
	IQR	60.00	15.00	60.00	15.00	60.00
	P		3.42, E-008	8.42, E-008	2.39, E-007	5.23, E-007

P values denote significance of change in values as compared to status at presentation. IQR indicates interquartile range.

bisphosphonates [1-6] appear to be the most promising. However, to date, there were no data regarding long-term efficacy of this novel therapy. Although Agarwala et al [6] have recently reported a favorable role of alendronate in AVNFH in 395 hips for 1 to 8 years of follow-up, the mean duration of assessment in this manuscript has been 4 years. We hereby, for the first time, have presented a retrospective assay of our 10-year experience with a cohort of 53 hips subjected initially to 3-year-long alendronate treatment.

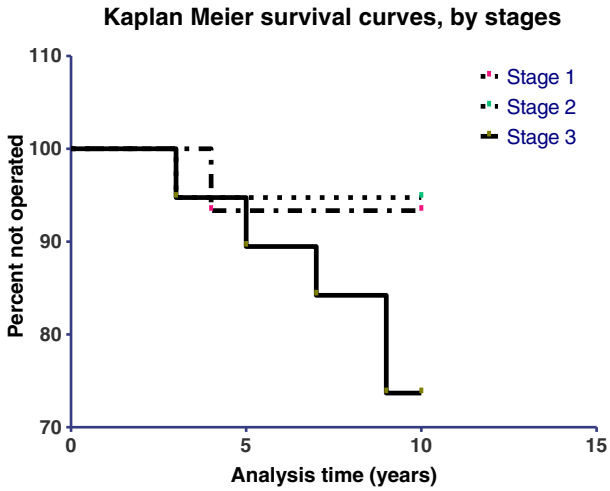

Fig. 3. Clinical survival analysis of AVNFH hips grouped according to the Ficat stage of avascular necrosis (AVN) at onset of the treatment.

Although several bisphosphonates have been in use in orthopedic practice, we used alendronate because it was the molecule that we had maximum experience with until the late 1990s. The natural progression of untreated AVNFH was known to last for about 3 years in most of the cases [7-9]. At the time of onset of our prospective study, safety was established for use of our dosage schedule only up to 3 years. We had therefore restricted the regimen to a maximum of 3 years or until clinical failure was noticed, whichever was earlier. Incidentally, the latest update of 2009 bisphosphonate-related osteonecrosis of jaw position paper published by the American Association of Oral and Maxillofacial Surgeons also allows the use of this drug for 3 years without increment in the risk of jaw osteonecrosis [10]. Because of financial constraints, the use of MRI was limited only for the cases with diagnostic dilemma even after plain radiography (Ficat stage 1). The varied nature of activities of daily living of Indian patients precluded the use of available, validated, functional scoring systems and forced us to include basic visual analog scores for pain and disability wherein the disability score was supposed to correlate with functional impairment in performing activities of daily living and occupation.

Of the 40 patients (53 hips), 3 (3 hips) had a history of alcohol abuse of which 1 continued using alcohol until the last follow-up of 7 years. Another 4 patients (5 hips) had received long-term glucocorticoids for various

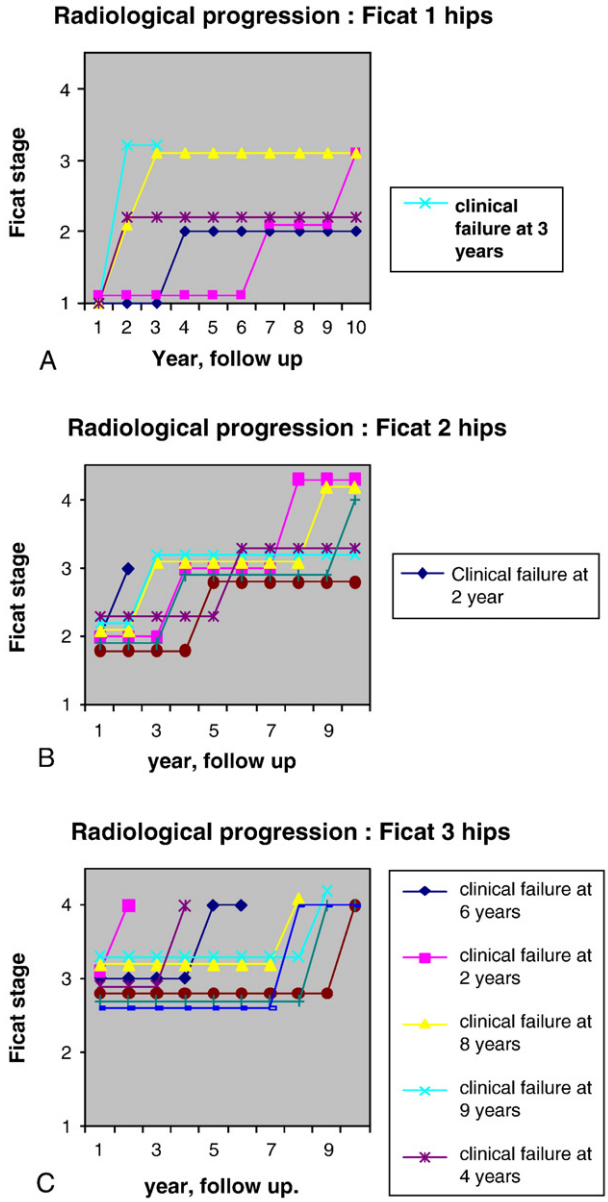

Fig. 4. (A) through (C). Radiologic progression of AVNFH hips in (A) Ficat stage 1, (B) Ficat stage 2, and (C) Ficat stage 3.

reasons, one of them being a case of systemic lupus erythematosus. She continued the use of steroids along with alendronate therapy until she underwent a total hip arthroplasty at 4 years of follow-up (Fig. 4C). In 33 of the 40 patients, no cause could be identified for AVNFH. The data about the etiology were thus too limited to draw any clinical or statistical conclusions.

Table 3. Radiologic Progression Noted at 10-Year Follow-Up

		At 10-year Follow-Up				
Ficat Stage at Onset	No. of Hips	In Stage 1	In Stage 2	In Stage 3	In Stage 4	No. of Hips Progressed
1	15	10	2	3	Nil	5 (33%)
2	19	–	12	4	3	7 (37%)
3	19	–	–	11	8	8 (42%)
Total	53	10	14	18	11	20(38%)

As seen in Table 1, the duration for which patients experienced hip pain was significantly higher ($P = 2.35$, E-0.6, unpaired t test) for stage 3 hips as compared with that for Ficat 1 and 2 stages together, implying that the earlier the diagnosis, the less is the structural damage to femoral head.

All clinical measures showed a trend of immediate and significant response to alendronate therapy (P values in Table 2) as well as maintenance of the betterment in clinical functions up to 3 years (Table 2 and Fig. 2), which was the period for which the drug was consumed. Although clinical functions showed a general trend of worsening after stopping ingestion of the drug, patients were found to be tolerating the decline well, as suggested by the fact that the number of cases needing arthroplasty was 3 in first 3 years and 4 in the later 7 years. Better tolerance of pain may probably be associated with the antiosteoporotic effects of long-term alendronate.

Earlier studies [7-9] reported an overall clinical progression rate of 77% to 98% in untreated AVNFH hips at an average of 3-year follow-up. Aron et al [11] have reported that more than 50% of the patients of AVNFH require total hip arthroplasty within 3 years. Mont and Hungerford [12], in their review of 21 studies involving 819 avascular necrosis (AVN) hips followed for a mean duration of 34 months, observed that 78% required further surgical intervention. Lai et al [4] have reported a 64% arthroplasty rate in 2 years in untreated hips, which reduced significantly to 3.5% in alendronate-treated group ($P < .001$). The total number of hips lost to arthroplasty in our study was 7 of the total 53 hips or 13% for a period of 10 years, standing in stark contrast to those reported in historical trials studying natural history of this relentless disease. The survival curves (Fig. 3) show a decline in stage 3 hips that is significantly greater than that in stages 1 and 2 hips (log-rank test, $P = .0414$), implying that the earlier the institution of this novel pharmacotherapy, the better the outcome.

Overall progression rates, however, may be influenced by the Ficat stage of AVNFH at presentation. We therefore isolated historical studies [13-18] that had studied progression of untreated AVNFH hips stage wise, using the same clinical-radiologic criteria as have been used in our study, and compared the outcome of our alendronate therapy to them. Stage-wise comparison of survival rates (Table 4) also reveals a reduction in clinical failure rates in all stages. Even in Ficat 3 (collapsed) hips, the failure rate is as low as 26%. On the contrary, it is widely held that once collapse sets in, no head-sparing modality is effective in AVNFH [19].

In 10 years, 20 (38%) of the 53 hips progressed on plain radiographic criteria of the Ficat-Arlet scale. In contrast, past studies [7-9,13] reported a radiographic progression rate of 68% to 75% at an average of 3-year follow-up. In the Mont and Hungerford review [12], of the 559 hips with radiologic follow-up, 74% progressed radiologically for 34 months. Stage-wise analysis reveals that the rate of progression in alendronate-treated AVN hips is less than that reported for untreated hips in all 3 stages (Table 4).

The timing of radiologic progression was also studied. Progression from stages 1 to 2 on the Ficat scale was seen as late as in sixth year of observation, whereas that from stages 2 to 3 was noticed in 1 case at 5 years (Fig. 4). We are therefore in agreement with the inference drawn in some of the recent studies [20-22] that clinical deterioration could occur long after the initial diagnosis of AVNFH.

A collapse rate of 29% in our study is much lower than the 80% collapse rate at 4 years, reported by Ohzono et al [19], and 76% collapse in 2 years, as observed by Lai et al [4]. The later study also reports a significant reduction of collapse rate with alendronate (to 7%; $P < .001$) for 24 months.

Collapsed femoral head invariably leads to eccentric loading of the joint, and Hartofilakidis and Karachalios [23] have shown that hips with eccentric degenerative changes undergo arthroplasty at an average period of 4 years after presentation for hip pain. In our group of 29 hips, after appearance of eccentric radiologic collapse, it took an average of 6.5 years for osteoarthritis to be evident on radiograms in 11 hips, whereas the remaining 18 hips were yet to develop radiologic arthritic changes even at last follow-up at 10 years. Alendronate thus may be effective in delaying progression of the disease even after collapse has set in.

Performing a retrospective study on a group of patients originally a part of a prospective study involves a huge challenge of tracing all the patients, specially those who seem to have lost to follow-up but could actually be either dead or have failed and hence not available for follow-ups. This model of study precludes changes to be made in the original institutional review board–approved study design, and hence the latest advances, howsoever relevant, cannot be included in the study. For example, because an

Table 4. Stage-Wise Comparison of Progression of AVNFH in our Trial vs Historical Data

	Clinical Failure		Radiologic Failure	
Ficat Stage	Pooled Data for Untreated Hips (%) [14-18]	Present Study (%)	Pooled Sata for Untreated Hips (%) [14-18]	Present Study (%)
Stage 1 [13,17,18]	85% of 20 hips for 24-27 mo	7% of 15 hips for 120 mo	89% of 36 hips for 24-27 mo	33% of 15 hips for 120 mo
Stage 2 [14-16,18]	96% of 29 hips for 18-63 mo	5% of 19 hips for 120 mo	62% of 121 hips for 18-63 mo	37% of 19 hips for 120 mo
Stage 3 [14-18]	95% of 21 hips for 18-63 mo	26% of 19 hips for 120 mo	84% of 104 hips for 18-63 mo	42% of 19 hips for 120 mo

MRI study could not be included in our original study design, the latest classification systems based on the site and size of the lesion, which have immense prognostic importance, could not be incorporated to study outcome of alendronate therapy. Moreover, although our study lacks an in-built control, we have compared response to alendronate with the progression rates in untreated hips, as reported in historical trials based on the same clinico-radiologic failure criteria. In spite these lacunae, the benefits of alendronate therapy at a follow-up of as long as 10 years are evident in our study.

In a nutshell, alendronate, given for 3 years, maintains its beneficial effects for as long as 10 years by changing the natural history of avascular necrosis of hips. Our long-term assessment makes a strong case for alendronate to be used as the drug of first choice in this relentlessly progressive disease, regardless of the stage in which patients present.

Acknowledgment

The authors thank Dr Abhiram Kasbe for performing statistical analysis in this manuscript.

References

1. Agarwala S, Sule A, Pai BU, et al. Study of alendronate in avascular necrosis of bone. J Assoc Phys India 2001;49:949.
2. Agarwala S, Jain D, Joshi VR, et al. Efficacy of alendronate, a bisphosphonate, in the treatment of AVN of the hip. A prospective open-label study. Rheumatology (Oxford) 2005;44:352 Epub 2004 Nov 30. Erratum in: Rheumatology (Oxford). 2005 Apr;44:569.
3. Agarwala S, Sule A, Pai BU, et al. Alendronate in the treatment of avascular necrosis of the hip. Rheumatology (Oxford) 2002;41:346.
4. Lai KA, Shen WJ, Yang CY, et al. The use of alendronate to prevent early collapse of femoral head in patients with non traumatic osteonecrosis. A randomized clinical study. J Bone Joint Surg Am 2005;87:2155.
5. Nishii T, Sugano N, Miki H, et al. Does alendronate prevent collapse in osteonecrosis of the femoral head? Clin Orthop Relat Res 2006;443:273.
6. Agarwala S, Shah S, Joshi VR. The use of alendronate in the treatment of avascular necrosis of the femoral head: follow-up to eight years. J Bone Joint Surg Br 2009;91:1013.
7. Merle d'Aubigne R, Postel M, Mazabraud A, et al. Idiopathic necrosis of the femoral head in adults. J Bone Joint Surg Br 1965;47:612.
8. Zizic TM, Hungerford DS. Avascular necrosis of bone. In: Kelly WN, Harris ED, Ruddy S, et al, editors. Textbook of Rheumatology. Philadelphia: WB Saunders; 1985; p. 1689.
9. Aaron RK, Gray RL. Osteonecrosis: etiology, natural history, pathophysiology, and diagnosis. In: Callaghan JJ, Rosenberg AG, Rubash HE, editors. The Adult Hip. Baltimore: Lippincott Williams and Wilkins; 2007; p. 463.
10. Ruggiero SL, Dodson TB, Assael LA, Landesberg R. American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws–2009 update. J Oral Maxillofac Surg 2009;67 (Suppl 5):2.
11. Aaron RK, Lennox D, Bunce GE, et al. The conservative treatment of osteonecrosis of the femoral head: a comparison of core decompression and pulsing electro magnetic fields. Clin Orthop 1989;249:209.
12. Mont MA, Hungerford DS. Non-traumatic avascular necrosis of the femoral head. J Bone Joint Surg Am 1995;77:459.
13. Bradway J, Morry B. The natural history of silent hip in bilateral atraumatic osteonecrosis. J Arthroplasty 1993;8: 383.
14. Hungerford DS, Zizic TM. The treatment of ischemic necrosis of the bone in systemic lupus erythematosus. Medicine 1980;59:143.
15. Musso ES, Mitchell SN, Schink-Ascani M, et al. Results of conservative management of osteonecrosis of the femoral head: a retrospective review. Clin Orthop 1986;207:209.
16. Ohzono K, Sugano N, Takaoka K, et al. Natural history of nontraumatic avascular necrosis of the femoral head. J Bone Joint Surg 1991;73B:68.
17. Steinberg ME, Hayken GD, Steinberg DR. The conservative management of avascular necrosis of the femoral head. In: Arlet J, Ficat P, Hungerford D, editors. Bone Circulation. Baltimore: Williams and Wilkins; 1984; p. 398.
18. Stulberg BN, Davis AW, Bauer TW, et al. Osteonecrosis of the femoral head. Clin Orthop 1991;268:140.
19. Ohzono K, Saito M, Sugano N, et al. The fate of nontraumatic avascular necrosis of the femoral head: a radiologic classification to formulate progress. Clin Orthop 1992;277:73.
20. Ito H, Matsuno T, Omizu N, et al. Mid-term prognosis of non-traumatic osteonecrosis of the femoral head. J Bone Joint Surg [Br] 2003;85-B:796.
21. Nam KW, Kim YL, Yoo JT, et al. Fate of untreated asymptomatic osteonecrosis of the femoral head. J Bone Joint Surg [Am] 2008;90-A:477.
22. Min BW, Song KS, Cho CH, et al. Untreated asymptomatic hips in patients with osteonecrosis of the femoral head. Clin Orthop 2008;466:1087.
23. Hartofilakidis G, Karachalios T. Idiopathic osteoarthritis of the hip: incidence, classification, and natural history of 272 cases. Orthopedics 2003;26:161.