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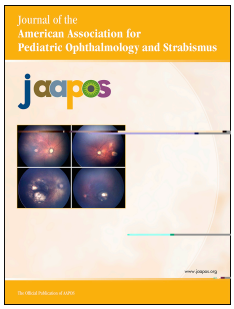


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# Long-term rate of evolution of age-related distance esotropia

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**Abstract**

*Purpose*

To evaluate the evolution of horizontal deviation and fusional amplitudes both at distance and at near in patients with age-related distance esotropia (ARDET).

*Methods*

The medical records of consecutive patients diagnosed with ARDET between January 2008 and March 2016 were reviewed retrospectively. Patients with at least 60 months' follow-up were eligible for inclusion. Horizontal deviation, fusional convergence amplitude, and fusional divergence amplitude both at distance and at near were compared.

*Results*

Of 131 cases reviewed, 31 patients were identified for inclusion. Median age at diagnosis was 73 years. Median distance esodeviation was $6^{\Delta}$ esotropia at initial examination (range, $2^{\Delta}$-$12^{\Delta}$ esotropia) and $8^{\Delta}$ eostropia at final examination (range, $2^{\Delta}$-$25^{\Delta}$ esotropia). Median near deviation was orthophoria at initial examination (range, $10^{\Delta}$ exophoria to $8^{\Delta}$ esophoria) and $4^{\Delta}$ esophoria at final examination (range, $4^{\Delta}$ exophoria to $14^{\Delta}$ esophoria). Median fusional divergence amplitude at distance was $4^{\Delta}$ at initial and at final examinations. At near, median fusional divergence amplitude was $8^{\Delta}$ at initial and at final examinations. Median fusional convergence amplitude at distance was $14^{\Delta}$ at initial examination and $12^{\Delta}$ at final examination. At near, median fusional convergence amplitude was $26^{\Delta}$ at initial and at final examinations. Base-out prisms were prescribed in all patients. In 23 patients the prism correction gradually increased. Strabismus surgery was performed in 3 patients.

*Conclusions*

Our patients with ARDET experienced a slight increase in distance esodeviation ($P < 0.001$),

whereas no significant change in fusional amplitudes was observed over time ($P \geq 0.05$).

Age-related distance esotropia (ARDET) is a small, acquired, comitant esodeviation with intermittent or constant horizontal diplopia occurring only at distance fixation.[1] At near, patients may present exophoria, orthophoria, or esophoria without double vision. This form of esotropia is observed in healthy individuals, usually >60 years of age, and is not associated with lateral rectus muscle underaction or with any currently known neurological pathology.[2,3] This type of esotropia is also defined as primary divergence insufficiency esotropia in older adults[4] or as sagging eye syndrome.[5]

In a previous study, we examined 87 patients with this condition, with availability of long-term follow-up date for 6 patients.[6] In this preliminary set of patients, we did observe a small progression of distance esodeviation and a mild decrease of fusional divergence amplitude. The current study evaluated the long-term progression of ARDET in a larger group of patients and the evolution of horizontal deviation and fusional divergence amplitude both at distance and at near.

**Subjects and Methods**

This study was approved by the Ethics Committee of the Antwerp University Hospital and adhered to the tenets of the Declaration of Helsinki. Beginning in January 2008, we recorded the data of patients with ARDET. By March 2016 our database included 131 patients. Consecutive patients from this database with at least 60 months' follow-up were identified. Patients were included if esotropia was at least $5^{\Delta}$ greater at distance than at near, onset of diplopia occurred after 60 years of age, abduction in both eyes was normal, and no suppression was detected. Patients with a history of childhood strabismus, previous strabismus surgery, coexisting vertical strabismus, cranial nerve palsies, supranuclear palsies, orbital trauma, thyroid eye disease, or myasthenia gravis were excluded.

Eye position was measured using the alternate prism cover test at distance (6 m) and at near (30 cm). Fusional amplitudes were measured for distance and near using horizontal prism bars. Fusional amplitudes were measured in the following order: (1) fusional divergence at distance, (2) fusional convergence at distance, (3) fusional divergence at near, and (4) fusional convergence at near. To measure divergence fusional amplitude, a horizontal prism bar (base-in) was placed in front of the right eye, while the patient fixated on a small target at distance or at near. The prism power was increased incrementally after fusion movement of the previous prism power, as follows:: 1-2-4-6-8-10-12-14-16-18-20-25-30-35-40. Once the patient noted diplopia, the break-up point was recorded.

Fusional convergence amplitude was measured similarly base-out prisms. No recovery points were measured, nor were vertical fusional amplitudes incorporated to break up proximal or tonic fusion. All fusional amplitude measurements and all binocular alignment measurements were performed with appropriate optical correction by the same investigator (DG). Ocular motility was evaluated clinically in all gaze directions, with an emphasis on lateral gaze. Measurements were recorded at each visit and the following comparative analyses were performed: initial visit versus visit at 5 years' follow-up, and initial visit versus last available visit.

**Results**

A total of 31 patients (10 males) who had a minimum follow-up of 5 years (average, 80.2 months; range, 60-161 months) were included. Follow-up was conducted between September 1999 and March 2016.

The average age of subjects 74.3 years (range, 64-85 years) at the initial examination and 89.7 years (range, 71-95 years) at final follow-up. Eleven patients were treated for hypertension,

2 for diabetes, 1 for arrhythmia, 1 for rheumatoid arthritis, and 1 for high cholesterol. Of the 31, 21 patients had bilateral pseudophakia, 4 had mild bilateral cataract, and 2 were treated for glaucoma. Ten eyes were emmetropic; 25 eyes, hyperopic (range, +2.75 D to +0.25 D); 27 eyes, myopic (range, −4.75 D to −0.25 D). Best-corrected visual acuity tested using the ETDRS chart was between 20/20 and 20/25 (logMAR +0.0 and +0.1) in 49 eyes, between 20/32 and 20/40 (logMAR +0.2 and +0.3) in 11 eyes, and was 20/50 (logMAR +0.4) in 2 eyes.

Median distance esodeviation was $6^{\Delta}$ esotropia at initial examination (mean with standard deviation, $5.52^{\Delta} \pm 2.64^{\Delta}$ esotropia; range, $2^{\Delta}$-$12^{\Delta}$ esotropia) and $8^{\Delta}$ esotropia at both 5-year follow-up (mean, $8.93^{\Delta} \pm 4.97^{\Delta}$ esotropia; range, $2^{\Delta}$-$25^{\Delta}$ esotropia) and at final examination (mean, $10.16^{\Delta} \pm 5.35^{\Delta}$ esotropia; range, $2^{\Delta}$-$25^{\Delta}$ esotropia). The distance esodeviation increased by $3.4 \pm 4.4^{\Delta}$ between the initial visit and final visit ($P < 0.001$; Figures 1 and 2). The increase was also significant ($P < 0.001$) when the initial visit was compared with the 5-year follow-up examination.

At near fixation, the median deviation was orthophoria ($0^{\Delta}$) at initial examination (mean, $0.13^{\Delta} \pm 4.44^{\Delta}$; range, $10^{\Delta}$ exophoria to $8^{\Delta}$ esophoria) and $4^{\Delta}$ esophoria at both the 5-year follow-up (average, $2.84^{\Delta} \pm 5.19^{\Delta}$; range, $6^{\Delta}$ exophoria to $14^{\Delta}$ esophoria) and at final examination ($3.26 \pm 5.39^{\Delta}$; range $4^{\Delta}$ exophoria to $14^{\Delta}$ esophoria). The box plot of Figure 3 shows that near deviation increase toward convergence ($2.71^{\Delta} \pm 4.68^{\Delta}$) is statistically significant ($P = 0.004$).

In all patients, the deviation remained horizontal; none of the patients developed a vertical deviation in the follow-up period.

Median fusional divergence amplitude at distance was $4^{\Delta}$ both at the initial examination (average, $3.93^{\Delta} \pm 2.98^{\Delta}$; range, $0^{\Delta}$–$10^{\Delta}$) and at the final examination (mean, $3.83^{\Delta} \pm 2.34^{\Delta}$; range, $0^{\Delta}$-$10^{\Delta}$) (Figure 4A). No statistically significant difference in fusional divergence amplitude at

distance ($-0.10^{\Delta} \pm 3.08^{\Delta}$) was observed over time ($P = 0.945$). At near, the median fusional divergence amplitude was $8^{\Delta}$ both at the initial examination (mean, $8.07^{\Delta} \pm 3.87^{\Delta}$; range, $4^{\Delta}$-$18^{\Delta}$), and at the final examination (mean, $7.87^{\Delta} \pm 3.62^{\Delta}$; range, $2^{\Delta}$-$16^{\Delta}$) (Figure 4B). No significant change in fusional divergence amplitude ($-0.21^{\Delta} \pm 3.91^{\Delta}$) was observed over time ($P = 0.383$).

The median fusional convergence amplitude at distance was $14^{\Delta}$ at the initial examination (mean, $12.87^{\Delta} \pm 5.38^{\Delta}$; range, 4–$22^{\Delta}$) and $12^{\Delta}$ at the final examination (mean, $12.64^{\Delta} \pm 4.45^{\Delta}$; range, $5^{\Delta}$-$22^{\Delta}$; Figure 5A). No significant difference in fusional convergence amplitude ($-0.40^{\Delta} \pm 6.46^{\Delta}$) was observed over time ($P = 0.748$).

At near, median fusional convergence amplitude was $26^{\Delta}$ both at the initial examination (mean, $27.00^{\Delta} \pm 8.52^{\Delta}$; range, $10^{\Delta}$ -$44^{\Delta}$) and at the final examination (mean, $25.16^{\Delta} \pm 7.54^{\Delta}$; range, $8^{\Delta}$-$42^{\Delta}$; Figure 5B). No statistically significant change in fusional convergence amplitude ($-2.21^{\Delta} \pm 8.21^{\Delta}$) was observed over time ($P = 0.359$).

In all patients, fusional divergence amplitude was present and, as expected, larger at near than at distance. At the initial examination, in 9 patients the fusional divergence amplitude was still large enough to correct the esodeviation at distance, meaning that fusional divergence amplitude at distance is larger than the esodeviation at distance. This finding correlates with the complaint of intermittent diplopia. At the final examination, only 3 patients had sufficient fusional divergence amplitude to correct their increased distance esodeviation.

At near fixation, all 12 patients who displayed an esophoria ($2^{\Delta}$-$8^{\Delta}$ esophoria) at the initial examination showed fusional divergence amplitude large enough to correct their esophoria. At the final examination, 16 patients were esophoric ($2^{\Delta}$-$12^{\Delta}$ esophoria) and 2 presented an esotropia (both $14^{\Delta}$ esotropia) at near. Two of the esophoric patients presented

intermittent horizontal diplopia at near and the 2 esotropic patients presented permanent horizontal diplopia because of insufficient fusional divergence amplitude at near.

Horizontal ductions and versions were full in all patients. None of the patients showed limited abduction. Alternate prism cover test at distance in lateral gaze did not change the esodeviation by more than $4^{\Delta}$.

All patients were successfully treated with prisms ranging from $2^{\Delta}$ to $12^{\Delta}$ base-out. Prism adaptation was first performed at 6 m and then evaluated at very far distance to ensure that no diplopia would occur when driving. In 23 patients, the prism correction increased over time ($4^{\Delta}$–$20^{\Delta}$), while in 8 patients, the prism correction remained the same for >5 years (60-78 months). Three patients underwent strabismus surgery (bilateral medial rectus recession) because of the large angle of distance esodeviation ($18^{\Delta}$ and $25^{\Delta}$). The initial esodeviation was $2^{\Delta}$ and $4^{\Delta}$. Surgery was always offered when the angle of the distance esodeviation was $>10^{\Delta}$. Also, 3 of the 76 patients with <5 years' follow-up were operated on (initial esotropia of $12^{\Delta}$, $14^{\Delta}$, and $16^{\Delta}$). Of the patients lost to follow-up, 3 had an initial distance esodeviation of $>10^{\Delta}$.

**Discussion**

To our knowledge, this is the first study to report the long-term evolution of ARDET and of fusional amplitudes in a large elderly cohort. The incidence of patients presenting with ARDET seems to have increased during the last 10 years.[7] A retrospective population-based cohort study about the incidence of adult-onset strabismus in Olmsted County, Minnesota, showed that divergent insufficiency esotropia was present in 10.6% of cases at a median age of 74 years (range, 19-92). The incidence rate increases with age, with a peak incidence in the eighth decade of life.[8] In our practice, we diagnosed ARDET earlier as a mild abducens nerve palsy or as a decompensation of a distance esophoria. Since 2008 we started to record data of elderly patients

with esodeviation at distance fixation and have examined and recorded 141 patients since. In 2013 we reported the clinical features of 87 patients with ARDET and discussed possible etiologies.[6] We also compared the fusional divergence amplitude to an age-matched control group of 56 elderly control subjects without distance esodeviation and observed smaller fusional divergence amplitude in the study patients (mean, $2.90^{\Delta}$; range, $2^{\Delta}$-$10^{\Delta}$) compared to the control group (mean, $8.25^{\Delta}$; range, 4–$16^{\Delta}$). At that time, we only had 6 patients with a follow-up of >5 years. We observed an increase in distance esotropia and a decrease in their fusional amplitude over time.

In this study, with a much larger cohort, we still confirm a statistically significant increase in distance esotropia ($P < 0.001$), but no significant decrease in fusional amplitudes was observed ($P > 0.05$). We also observed that the deviation especially increased after 7 years, but the population is too small to make any conclusion on this observation. All patients presented normal fusional convergence amplitudes for distance and for near, and smaller fusional divergence amplitudes. In all patients, the divergence amplitudes were larger for near than for distance, but this is normal for all ages.[9-10] Because fusional amplitudes over the years do not change but the esodeviation increases for distance and for near, patients become progressively less able to compensate for their increasing deviation, which results in greater horizontal diplopia at a shorter distance. Oatts and Salchow[10] retrospectively evaluated the fusional amplitudes in 15 of their 20 study patients with ARDET and observed deficient fusional divergence amplitude in most but not in all patients with ARDET. Nine patients had a fusional divergence amplitude, which was large enough to correct their esodeviation at distance. Bothun[11] observed an absence of divergence amplitudes at distance in 5 of 8 patients. (It was not reported how fusion was tested.) Wiggins and Baumgartner[12] retrospectively evaluated 17 patients with divergence

weakness, 16 of whom were over 60 years of age. All had $7^{\Delta}$ or less of fusional divergence at distance. Only 1 patient had a follow-up of 4 years with an increase of esotropia at distance from $10^{\Delta}$ to $19^{\Delta}$ and no significant change in the near deviation. Palomo Alvarez and colleagues[13] found in a large nonclinical population (271 subjects) that break values for fusional vergence were comparable between age groups but measured reduced recovery values in older individuals. Using Risley rotary prisms, the mean base-in recovery decreased by $2.5^{\Delta}$ between the youngest (21-30 years) and the oldest (17-80 years) age groups, while mean base-out recovery decreased by $3.3^{\Delta}$. In our study we measured break values and used prism bars. They also observed that the mean heterophoria value for distance fixation was exophoric except in their 71- to 80-year-old group, which was esophoric.

Although the etiology of ARDET is still not clear, it is likely secondary to involutional changes within the orbit[14]; most notably, sagging and inferior displacement of the lateral rectus muscles and its pulleys, caused by tendon laxity due to degeneration.[5-15] Recent studies of Chaudhuri and Demer[16-18] have shown that sagging and bilaterally symmetrical downward displacement of the lateral rectus pulleys may symmetrically reduce supraduction and may cause esodeviation and horizontal diplopia at distance. On the other hand, a bilaterally asymmetrical lateral rectus sag may result in hypotropia and excyclotropia of the eye with the greater sag, causing cyclovertical diplopia.

We believe that ARDET is part of the sagging eye syndrome and that, the longer lateral rectus muscles weaken with age more than the shorter medial rectus muscles, resulting in a slowly progressive esodrift for distance and at a later stage also for near. All our study patients had a pure horizontal deviation and in no case did a patient with ARDET develop a vertical deviation over the follow-up period. Because the fusional convergence amplitude is larger, small

to moderate progressive exodeviations can be corrected more easily. The fusional divergence amplitude, however, is much smaller, especially at distance; thus, when the eyes deviate progressively inward, patients are unable to compensate for it resulting in horizontal diplopia especially at distance. Fusional divergence amplitude was present in all patients, although these were not large enough for the majority of patients to correct the acquired esodeviation at distance. Patients with higher fusional divergence amplitudes complain initially about intermittent horizontal diplopia, more pronounced on lateral gaze or only at very far distance. As the esodeviation progresses over time, the point at which the horizontal diplopia occurs gets closer, which may even result in diplopia at near.

Out study was limited by the fact that the majority of the patients have a follow-up of <5 years. Also, we lost 24 patients to follow-up.

We evaluated the long-term progression of ARDET patients, focusing on the evolution of horizontal deviation and fusional divergence amplitudes at distance and at near. Esodeviation at distance increased slowly over time ($P < 0.001$). At near, the deviation also shifted toward convergence ($P = 0.003$). No vertical deviations developed during our follow-up (60-161 months). No significant change in fusional amplitude (convergence and divergence) at distance nor at near was observed over time ($P > 0.05$). Divergence fusional amplitude was present in all patients, although not large enough to correct the slowly progressive esodeviation at distance. Prism correction will be in most cases the first therapy, with recourse to surgery when the deviation becomes larger.

**Literature Search**

The Web of Science and PubMed databases were searched on December 15, 2016, using the following terms: *ARDET*, and *age-related* AND *distance esotropia*.

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**Legends**

**FIG 1.** Esodeviation in prism diopters at distance (6 m) in 31 patients. Gray bars are the deviation at first visit, black bars at last visit. Patients 1-18 had a follow-up of 60-71 months; patients 19-24, 72-95 months; patients 25-28, 96-119 months; and patients 29-31, of >120 months. *PD*, prism diopter.

**FIG 2.** Box-and-whiskers plots of distance esodeviation in prism diopters at first and final visit ($3.41^{\Delta} \pm 4.35^{\Delta}$; $P < 0.001$).

**FIG 3.** Box-and-whiskers plots of the near deviation in prism diopters at first and final visit ($2.71^{\Delta} \pm 4.68^{\Delta}$; $P = 0.004$). The range from $-10^{\Delta}$ to $0^{\Delta}$ represents exophoria; from $0^{\Delta}$ to $15^{\Delta}$, esophoria.

**FIG 4.** Box-and-whiskers plots depicting the fusional divergence amplitude in prism diopters measured with incremental prism bars at distance (6 m) and near (30 cm). A, At distance, at first and at final visit ($-0.10^{\Delta} \pm 3.08^{\Delta}$; $P = 0.945$). B, At near, at first and final examination ($-0.21^{\Delta} \pm 3.91^{\Delta}$; $P = 0.945$).

**FIG 5.** Box-and-whiskers plots depicting the fusional convergence amplitude in prism diopters measured with incremental prism bars at distance (6 m) and near (30 cm). A, At distance, at first and final visit ($-0.40^{\Delta} \pm 6.46^{\Delta}$; $P = 0.748$). B, At near, at first and final visit ($-2.21^{\Delta} \pm 8.21^{\Delta}$; $P = 0.359$).