

## Chapter 4

### **Patients and characteristics**

## Period of study and number of patients

During a three and a half year period (from January 1994 to June 1997) 128 patients, suspected of having Menière's disease, were admitted for four days at the Department of Otorhinolaryngology of the University Hospital Groningen, a tertiary referral center. According to the Definition Menière Groningen, these patients had a history of vertigo attacks (at least two), suffered or had suffered from tinnitus and had a sensorineural hearing loss of at least 20 dB at one of the audiogram frequencies. During the admission they were subjected to a wide range of tests, called the Groningen Diagnostic Protocol.

## Exclusion of patients

In this study 17 patients (13 female and 4 male) had to be excluded from the study. According to the Definition Menière Groningen these patients were not diagnosed as patients with Menière's disease after completing the Groningen Diagnostic Protocol. These patients and their diagnoses are listed in table 1.

*Table 1. Drop-outs through the Groningen Diagnostic Protocol*

Diagnosis of excluded patients	number of patients	
- Balance disorder of central origine	2	(2f)
- Labyrinthitis	1	(f)
- Idiopathic sudden sensorineural hearing loss (ISSHL)	1	(f)
- Acoustic neurinoma	1	(f)
- Labyrinthine otosclerosis	2	(f)
- Noise induced hearing loss	1	(m)
- Tympanosclerosis	1	(f)
- Absence of sensorineural hearing loss in pure-tone audiogram	6	(3f,3m)
- Absence of vertigo in history	1	(f)
- Intake/follow-up form missing	1	(m)
m = male, f = female	total	17 (13f, 4m)

The two patients with aspecific dizziness of a central origine had psychological complaints accompanied by hyperventilation. One patient suffered from a chronic mastoiditis complicated by a labyrinthitis and was treated by a mastoidectomy and intravenous antibiotics. One patient had a non-fluctuating hearing loss and a short single period of vertigo and was diagnosed as idiopathic sudden sensorineural hearing loss (ISSHL). Transotic extirpation of a tumor with a diameter of 2 cm was performed on one patient with an acoustic neurinoma. Two patients with a sensorineural hearing loss, tinnitus and fluctuating vertigo received the diagnosis of labyrinthine and tympanic otosclerosis and underwent a stapedotomy. In one patient suffering from sensorineural hearing loss and tinnitus tympanosclerosis was finally diagnosed. Two patients with a high frequency sensorineural hearing loss and tinnitus were diagnosed as noise induced hearing loss. According to the Definition Menière Groningen, six patients were excluded because they did not have a sensorineural hearing loss of at least 20 dB at one of the pure-tone audiogram frequencies.

## Patients characteristics

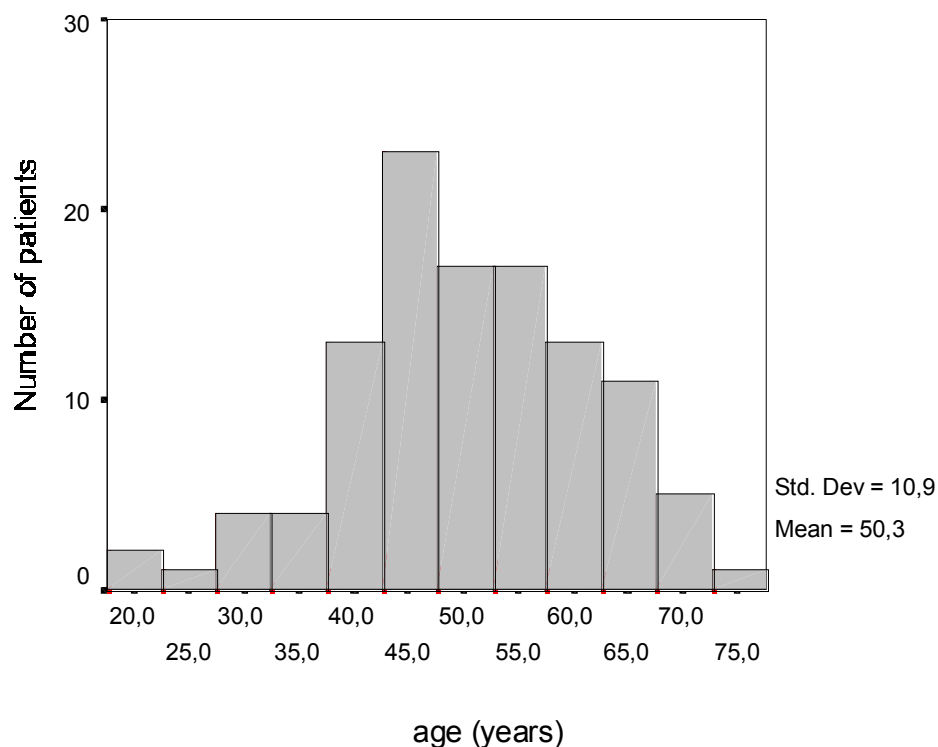
**Table 2.** Gender distribution, affected and unaffected ears

Gender	n (ears)	Percentage (%)
All patients		
affected ears	71	32
unaffected ears	151	68
all ears	222	100
Male		
affected ears	75	65
unaffected ears	39	35
all ears	114	100
Female		
affected ears	76	70
unaffected ears	32	30
all ears	108	100

Based on the criteria of the Definition Menière Groningen finally 111 patients were diagnosed with Menière's disease. 57 Patients were male (51%) and 54 patients were female (49%). There were 151 affected ears and 71 unaffected ears (table 2).

### Age

The age distribution of the population is shown in figure 1. The mean age was 50.3 ( $\pm 10.9$ ) years. This was the mean age at the time of the hospital admission for the Groningen Diagnostic Protocol. There was no significant difference in age between male and female ( $p=0.77$ , two samples T-Test, significance level  $p=0.02$ ). The youngest patient studied was 19 years old, the oldest patient was 77 years old.



**Figure 1.** Histogram: age distribution of the population ( $n=111$ ).

### Unilaterally and bilaterally affected

In our population 71 patients had only one affected ear. This is 64% of the total population. Thirty-nine of these patients were male and 32 were female. The remaining 40 patients suffered from bilateral Menière's disease. This is 36% of the total population. Eighteen of these patients were male and 22 were female. In unilaterally and in bilaterally affected patients there was no significant difference in the number of male and female patients (T-Test, significance level  $p=0.02$ ). On admission the mean age of the unilaterally affected patients was 50.1 ( $\pm 11.4$ ) years and of the bilaterally affected patients 50.7 ( $\pm 10.2$ ) years as summarized in table 3. The difference in age at

the time of the hospital admission was not statistically significant (two samples T-Test,  $p=0.77$ ).

**Table 3.** Age distribution: male/female and uni-/bilaterally affected patients.

Patients	Mean age at first time of affection	Standard deviation	Mean age at the time of admission to hospital	Standard deviation	Duration of disease	Standard deviation
	years	years	years	years	years	years
All	42.8 (17-68)	11.5	50.3 (19-77)	10.9	7.5 (0.2-30)	6.7
Unilaterally affected	43.5 (17-68)	12.1	50.1 (19-77)	11.4	6.4 (0.2-28)	6.1
Bilaterally affected	41.7 (17-60)	10.7	50.7 (28-68)	10.2	9.0 (0.5-30)	7.2
Male	41.7 (17-66)	12.0	49.3 (19-77)	11.0	7.6 (0.2-30)	6.7
Female	44.0 (21-68)	11.0	51.4 (22-68)	10.8	7.4 (0.5-30)	6.7

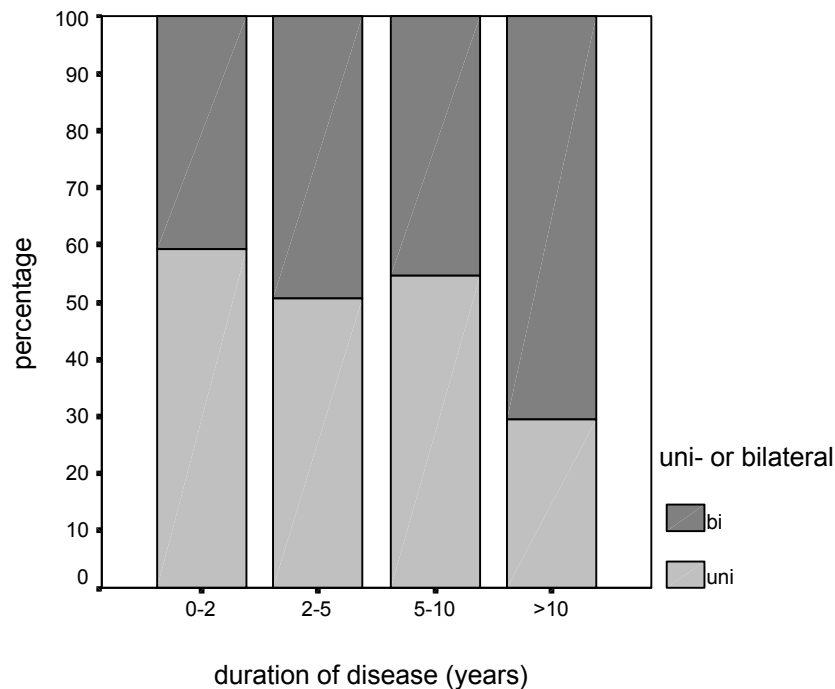
#### Duration of the disease and symptoms

In unilaterally affected patients the duration of the disease and the duration of affection of the affected ear was defined as the period between first appearance of one of the Menière symptoms and the admission into the hospital. The duration of the disease in a bilaterally affected patient was equal to the duration of affection of the first affected ear of the patient. The duration of affection of the contralateral ear was defined as the period from the date of first occurrence of either hearing loss (documented) or tinnitus to the date of the hospital admission.

After defining duration of affection we were able to determine the age of the patients at the first time of affection (table 3). At the start of the disease the mean age of the total Menière population was 42.8 ( $\pm 11.5$ ) years. At the start of the disease the mean age of the unilaterally affected patients was 43.5 ( $\pm 12.1$ ) years. The mean age of the bilaterally affected patients was 41.7 ( $\pm 10.7$ ) years, which indicated that the bilaterally affected patients were 1.8 years younger than the unilaterally affected patients at the start of the disease. This difference was not statistically significant ( $p=0.41$  two samples T-Test, significance level  $p=0.02$ ). For the male subgroup the age of first affection was 41.7 ( $\pm 12.0$ ) years and for the female subgroup 44.0 ( $\pm 11.0$ ) years (no significant difference,  $p=0.30$ , two samples T-Test, significance level  $p>0.02$ ).

At the time of the hospital admission the total group of patients was 7.5 years older. At the hospital admission the mean duration of unilateral Menière's disease was 6.6 ( $\pm 6.1$ ) years and the duration of bilateral Menière's disease was 9.0 ( $\pm 7.2$ ) years. This

difference was statistically significant ( $p=0.036$ , Wilcoxon signed-rank test due to non-normal distributions, significance level  $p=0.05$ ).



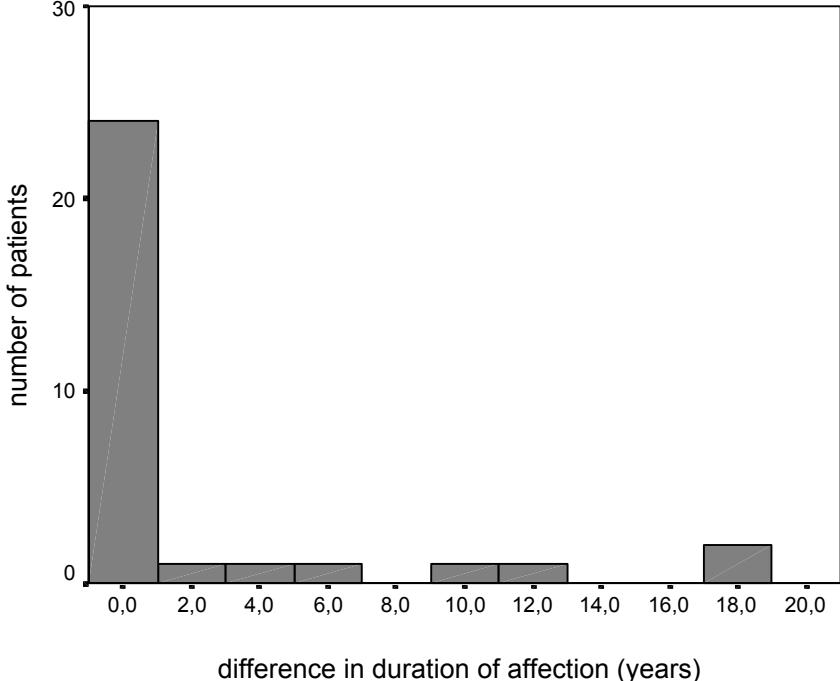
**Figure 2.** Duration of disease in uni- and bilaterally affected patients. *bi* = bilaterally affected patients ( $n=40$ ), *uni*= unilaterally affected patients ( $n=71$ ).

In figure 2 the duration of the disease was divided into four groups (0-2, 2-5, 5-10 and >10 years). The gradual increase in the (relative) number of bilaterally affected patients may suggest that the disease first starts unilaterally and will become bilateral in a later stage. In order to check this hypothesis we studied the bilaterally affected group of patients separately. For each patient we compared duration of the disease in the first affected ear (9.0 ( $\pm 7.2$ ) years) with duration of the disease in the ear affected last (7.3 ( $\pm 7.2$ ) years). This difference in duration between the first and the last affected ear was not statistically significant ( $p=0.289$ , independent samples T-Test with significance level  $p=0.02$ ). Furthermore, we observed that the difference in duration between the two ears rarely exceeded one year (figure 3).

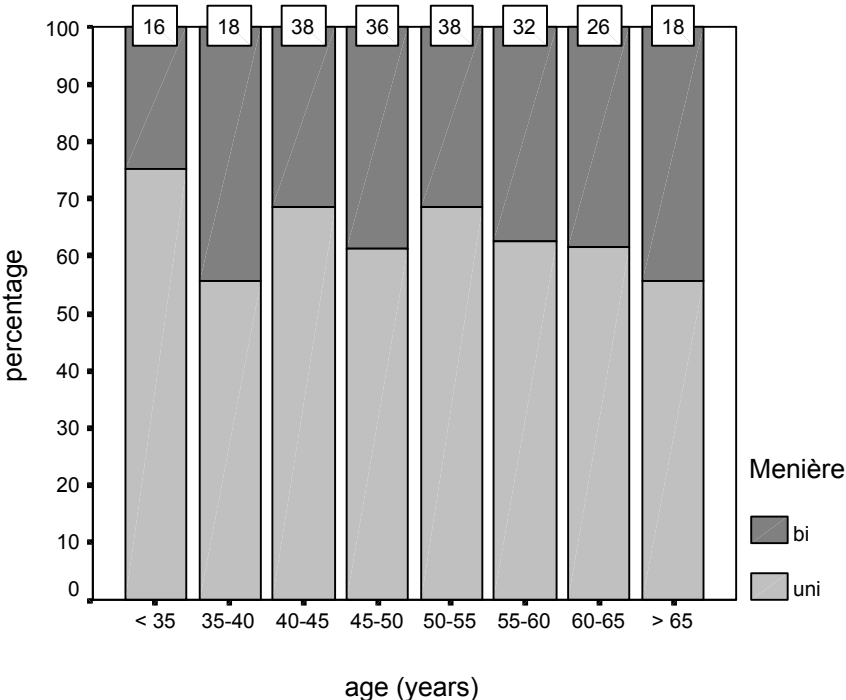
We already concluded that there was no difference in the mean age between uni- and bilaterally affected patients at the time of the admission. Figure 4 shows that there is no influence of age on having uni- or bilateral Menière's disease.

We also examined the difference in duration between the first and the last symptom of the trias as given in the Definition Menière Groningen of each affected ear ( $n=151$ ). This is illustrated in the histogram of figure 5. There was one ear missing because of an incomplete questionnaire. In 99 ears (66%) all the symptoms were present within

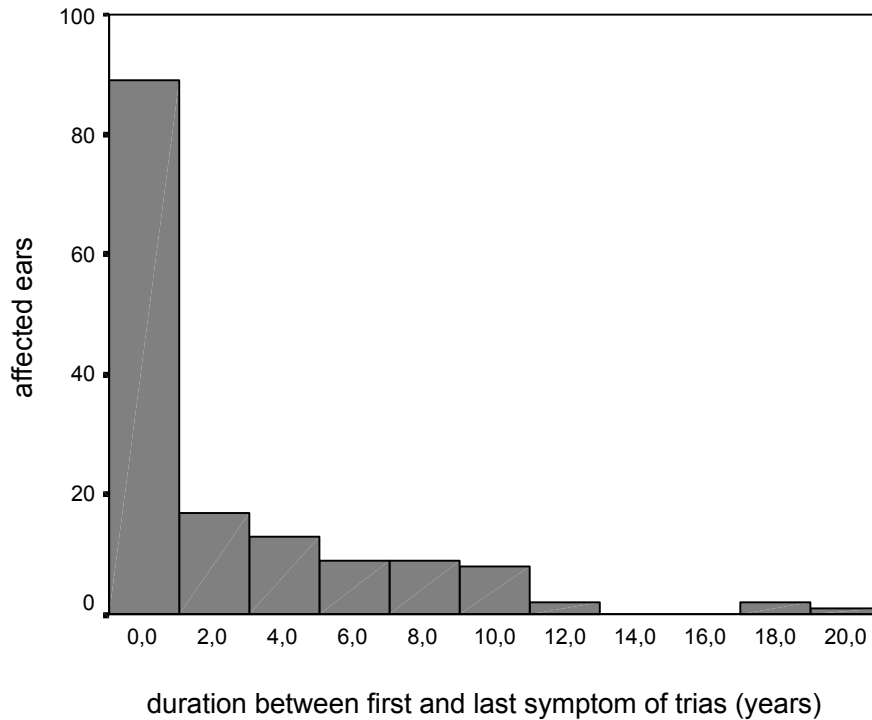
one year (figure 5). In only five ears it took more than ten years before all symptoms were present.



**Figure 3.** Histogram: difference in duration of affection between first and last affected ears (bilaterally affected patients, n=40, mean=1.7 years, SD=4.5).



**Figure 4.** Influence of age on uni-/bilateral affection, all ears (n= 222). Horizontally the age is divided in 5-year-groups and vertically the percentage of uni/bilaterally affected patients per group is listed. At the top of each bar the number of ears is given (white boxes).



**Figure 5.** Histogram: difference in duration between the first and the last symptom of the trias as given in the Definition Menière Groningen (affected ears,  $n=150$ , mean= 2.3 years,  $SD=3.87$ ).

In table 4 the mean durations of separate symptoms of all affected ears are listed. In our group, the duration of vertigo was 6.6 ( $\pm 6.6$ ) years. Hearing loss as well as tinnitus were present for 6.2 years ( $\pm 6.3$  years for hearing loss and  $\pm 6.4$  years for tinnitus). A sensation of aural pressure/fullness (if present) had an mean duration of 4.5 ( $\pm 6.4$ ) years.

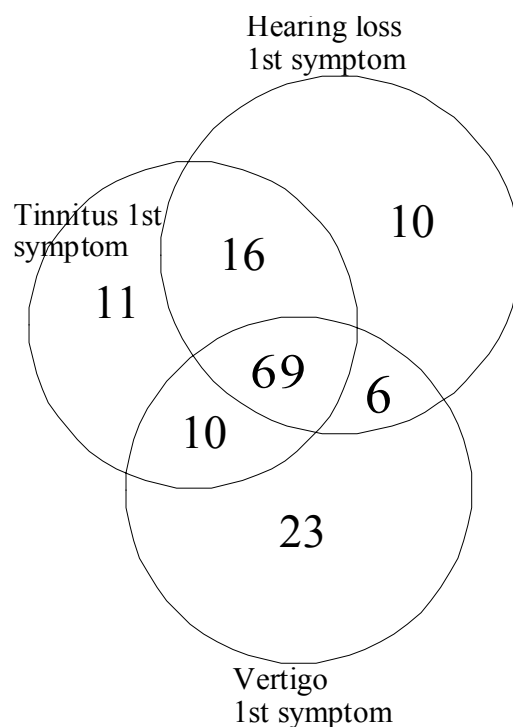
**Table 4.** Affected ears, duration of symptoms (years,  $n=151$ ).

	Hearing loss	Tinnitus	Vertigo	Aural pressure
	Duration (years)	Duration (years)	Duration (years)	Duration (years)
Mean	6.1	6.2	6.6	4.5
Standard deviation	6.3	6.4	6.6	6.4
Range	0-30	0.1-30	0.2-30	0-30

Furthermore, we studied the initial presentation of the separate symptoms in all affected ears. In 101 ears (70%) the hearing loss was the initial symptom of the disease. In 9 ears (6%) it was the last symptom present. In 106 ears (73%) tinnitus was



among the first symptoms and appeared as the last symptom in 5 ears (4%). In 70 ears (48%) aural pressure/fullness was presented at the onset. In 48 ears (33%) this symptom was the last presenting symptom. In 108 ears (75%) vertigo was among the first complaints and in 10 ears (7%) it appeared the last. In figure 6 the number of affected ears (n=145) is illustrated for each first presenting symptom (hearing loss, tinnitus and vertigo) or a combination of the symptoms. In 69 (48%) ears all three symptoms were present at the start of the disease. Two of the three symptoms were observed in 42 ears (29%). In 101 ears (70%) at least two symptoms were present at the beginning of the disease. The disease started with only one symptom in 44 ears (30%). In 56 ears (39%) aural fullness was present together with the trias (hearing loss, tinnitus and vertigo) at first appearance of the disease.



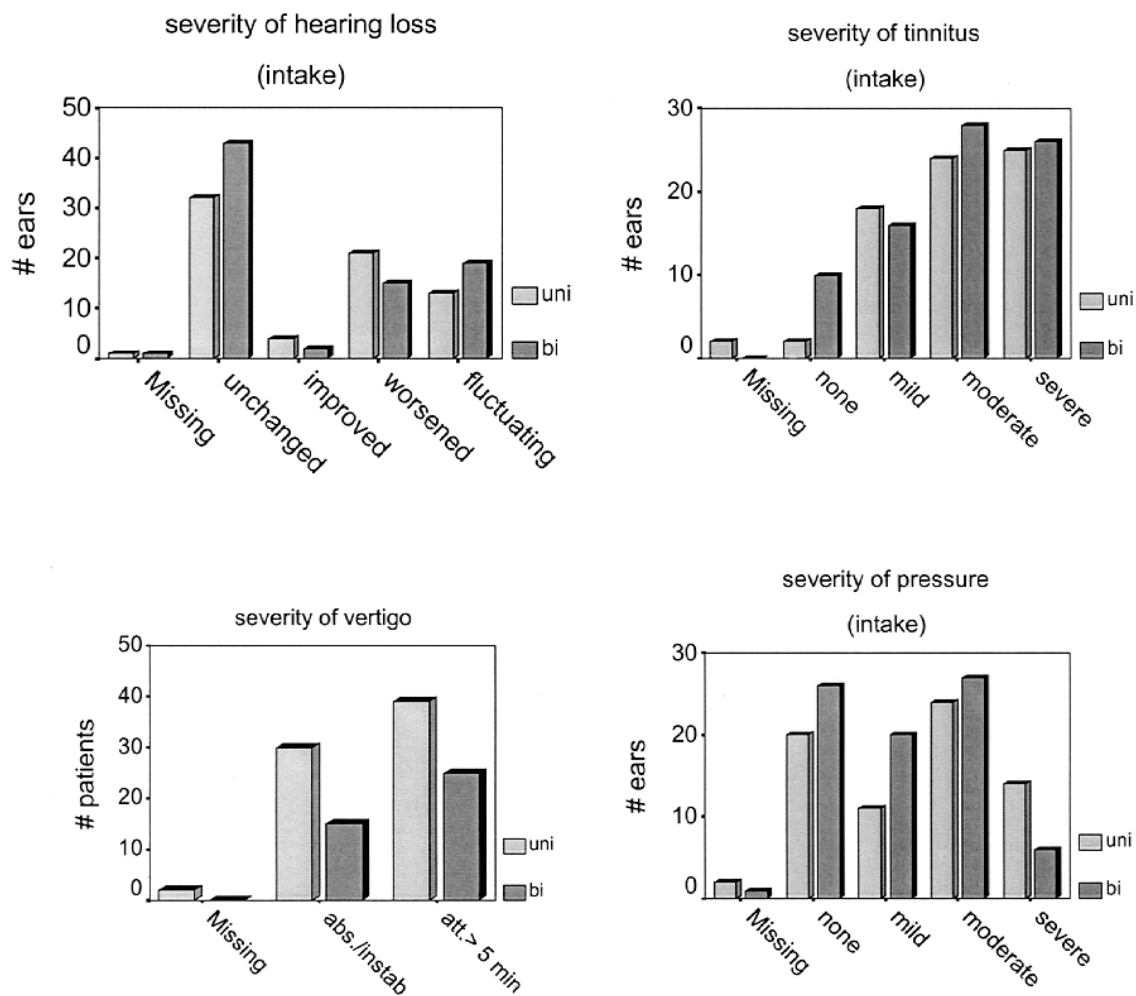
**Figure 6.** Affected ears, Venn diagram: distribution of affected ears related to first presenting symptom or combination of symptoms (hearing loss, tinnitus and vertigo, n=145).

#### Duration in relation to severity of symptoms

Another aspect of the symptom score we investigated was the influence of the duration of affection on the severity of the symptoms. We concluded that there was no statistical difference in severity of the separate symptoms hearing loss (p=0.34), tinnitus (p=0.18), vertigo (p=0.07) and/or aural pressure (p=0.99) in the affected ear between groups of ears with short ( < 2 years) and long ( ≥ 2 years) duration of the disease (Pearson Chi-square test, significance level p=0.02).

## Severity of symptoms

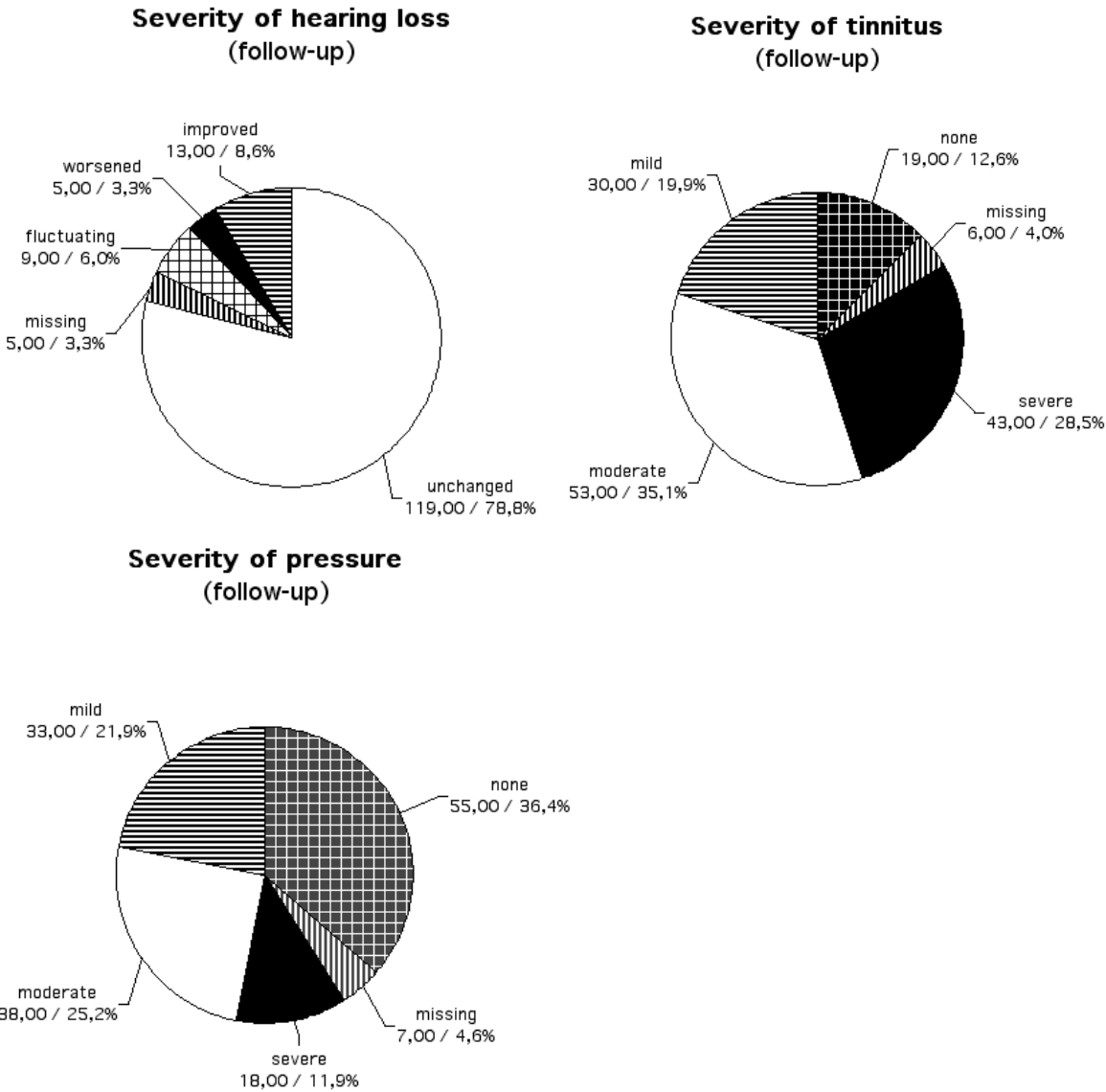
The severity of symptoms was scored with a questionnaire which was part of the score form (appendix chapter 2). Figure 7 shows the symptom scores at the 'intake'. Of all affected ears (n=151) 21% exhibited a hearing loss over the last three months characterized by the patient as 'fluctuating', 24% as worsened and only 4% as improved. In about half of the affected ears (50%) the hearing loss over the last 3 months was unchanged. Tinnitus was noticed in 91% of all affected ears. 22% suffered from mild, 34% moderate and 34% from a severe tinnitus. 59% of the patients suffered from vertigo attacks lasting for more than 5 minutes over the last three months. In the three months prior to the 'intake' aural fullness/pressure in the ear was present in 68% of all affected ears (mild 21%, moderate 34%, severe 13%). There were no significant differences in severity of hearing loss ( $p=0.28$ ), tinnitus ( $p=0.17$ ) and aural pressure/fullness ( $p=0.1$ ) between uni- and bilaterally affected ears (Pearson Chi-square test, significance level  $p=0.02$ ). Vertigo was scored per patient. There was no significant difference in vertigo between uni- and bilaterally affected patients ( $p=0.54$ , Pearson Chi-square test, significance level  $p=0.02$ ).



**Figure 7.** Symptom scores at the 'intake', severity over the last three months. (uni=unilaterally affected patients, bi=bilaterally affected patients, abs./instab.=absent or instability/attacks lasting less than 5 minutes, att.> 5 min=attacks lasting more than 5 minutes).

**Correlation between symptoms**

To investigate a possible correlation between the severity of the symptoms we made cross tabulations of the symptom scores at the ‘intake’. Statistics were performed with a two tailed Pearson Correlation (significance level,  $p=0.02$ ,  $n=151$ ). The severity of vertigo did not correlate with the severity of the other symptoms (hearing loss, tinnitus, aural pressure/fullness). The severity of hearing loss in the affected ears correlated with the severity of tinnitus ( $p=0.002$ ) and aural pressure/fullness ( $p<0.001$ ), but not with severity of vertigo ( $p=0.87$ ). For a ‘fluctuating’ hearing loss a shift to ‘severe’ tinnitus was found ( $p=0.002$ ). Furthermore in the affected ears there was a statistically significant correlation between tinnitus and aural pressure/fullness ( $p<0.001$ ).



**Figure 8.** Pie charts: Symptom scores of affected ears at the ‘follow up’, severity of hearing loss, tinnitus and aural fullness/pressure (over the last 4 days/period of admission).

### Effect of hospital admission on severity of symptoms

To study whether the hospital admission had an effect on the severity of the Menière symptoms the scores of the ‘intake’ and ‘follow-up’ had to be compared (figure 7 and 8). Statistics were performed with a Wilcoxon Signed Rank Test (significance level,  $p=0.02$ ).

At the time of the ‘follow-up’, 78.8% of all the affected ears had an ‘unchanged’ hearing loss, 8.6% an improved, 3.3% a worsened and 6.0% a fluctuating hearing loss ( $n=151$ , figure 8). There was no statistically significant change in severity of hearing loss score ( $p=0.35$ ).

The perceived tinnitus score at the ‘follow-up’ was as follows: 12.6% none, 19.9% mild, 35.1% moderate and severe 28.5% ( $n=151$ , figure 8).

For aural fullness/pressure this ‘follow-up’ score was: 36.4% none, 21.9% mild, 25.2% moderate and 21.2% severe ( $n=151$ , figure 8). There was a statistically significant improvement of both tinnitus and aural fullness/pressure score at the end of the hospital admission in both cases ( $p= 0.002$ ).

## Discussion

As part of the Definition Menière Groningen the Groningen Diagnostic Protocol was used to diagnose patients suspected of having Menière’s disease and to exclude other pathology. The fact that 17 out of 128 patients finally did not have Menière’s disease is illustrative for the usefulness of the Groningen Diagnostic Protocol as part of the Definition Menière Groningen.

### Patient characteristics

In our population the number of male and female Menière patients was equal. Of all included patients 36% suffered bilateral disease. This corresponds well with Paparella and Griebie who reported an incidence of bilateral disease of 30-50% in their study population [1]. In Japan Kodama reported a similar percentage of bilateral disease [2]. The first manifestations of Menière’s disease as described in the literature usually begin between the age of 30 and 60 years. In our population the disease started at a mean age of 42.8 years. The mean age at admission of the studied group was 50.3 years which was also similar to the literature. The youngest patient was 19 at first appearance of the symptoms and the oldest was 77 years old.

The age at the onset of the disease is also comparable to values mentioned in literature [3]. Comparing the patient characteristics of the studied cohort with the literature the studied patient group can be regarded as representative with a high external validity.

## Duration

In the literature there is still no consensus in defining the start of the disease. Some authors define the beginning of the disease as the moment at which all symptoms of the triad are present for the first time. In a retrospective study Pfaltz [4] found a complete triad initially present in only 25% of all cases (n=100). He defined the onset of the disease as the onset of the first symptom, comparable to our study. In a study of Ralli et al [5] Menière's disease appeared with the classic triad of symptoms in about 1/3 of cases. Watanabe [6] and Gentine [7] reported a much higher incidence of initial presence of the triad (50-55%). In our population we noticed that within one year 66% of all patients had all symptoms.

Long-term studies have shown that up to 50% of all unilateral affected patients will eventually develop symptoms from the opposite ear [8,9,10]. Paparella and Griebie found that of those persons with bilateral disease 50% experienced symptoms from the opposite ear within a period of 2 years, with an additional 27 % having symptoms after 5 years [1]. At present it is still not known whether disease in one ear directly leads to involvement of the opposite ear at a later date, or whether bilaterality must be regarded as a separate entity.

In our patient group, the gradual increase in the (relative) number of bilaterally affected patients with duration (which is in agreement with the 2.4 years extra mean duration in the bilaterally affected group) seems to support the hypothesis that the disease first starts unilaterally and will become bilateral in a later stage [11,12] (figure 2). However, the difference in duration between the first and the last affected ears in the bilaterally affected group was not statistically significant. Furthermore, we observed that the difference in duration between the two ears rarely exceeded one year (figure 3). In contrast to the previously mentioned literature these data make it rather unlikely that the difference in duration found between uni- and bilaterally affected patients in our population was caused by a gradual change-over of unilateral disease into bilateral disease.

In this study there was no uniform initial presentation of the separate symptoms. Vertigo usually was the first presenting symptom (75%), but hearing loss (70%) and tinnitus (73%) scored an almost comparable percentage. Our results partly disagree with the statement of Matsuoka et al that hearing loss is the first occurring symptom [12]. At the start of the disease almost half of the patients suffered from the complete triad of symptoms. None of the three symptoms was among the first occurring in all patients. This implies that no single symptom can be used to define the onset of the disease.

In 39% of all patients this triad of symptoms was accompanied with a sensation of aural fullness/pressure. The fact that aural fullness/pressure occurred in 82% of all affected ears indicates that it is a relevant symptom in Menière's disease.

### Duration of Menière disease in relation to severity of symptoms

The severity of symptoms did not significantly depend on duration of Menière's disease in our group of patients. This implicates that the idea that symptoms might worsen or improve over the time can not be substantiated in our patients group [11,13,14].

### Correlation between symptoms

A strong correlation was found between aural fullness/pressure sensation and tinnitus, implicating that a more severe sensation of aural fullness/pressure corresponded to a more severe sensation of tinnitus in the ear. The presence of aural fullness/pressure has no additional value for the definition of Menière's disease, because patients with aural pressure sensation were almost automatically included because of having tinnitus. This is partly in concordance with the 1995 definition of Menière's disease of the AAOO-HNS where either aural fullness or tinnitus (or both) need to be present [15].

Patients with a fluctuating hearing loss generally had a more severe tinnitus and aural fullness/pressure sensation. In contrast an 'unchanged' hearing was related to a 'mild' score in aural pressure/fullness. These findings may support the hypothesis that an actual endolymphatic hydrops is responsible for an increase of symptoms as hearing loss fluctuation, tinnitus and aural pressure, possibly indicating to an instable Menière's disease [16], although no similar relation could be found with the symptom vertigo.

### Effect of hospital admission on severity of symptoms

Of all patients 79% scored their hearing as 'unchanged' during the hospital admission of four days. This could be expected on the basis of the short period of only four days over which the 'follow-up' extended. After four days of admission a relief in the mean symptom score was noticed in the group of the affected ears. A significant decrease in the symptom scores of tinnitus and aural pressure/fullness sensation was observed after hospital admission for the Groningen Diagnostic Protocol. These findings could imply that the hospital admission had a therapeutical effect, although the consistency of this effect on the long term is only speculatively. The hospital admission caused a release in tinnitus and aural pressure/fullness, possibly by reducing stress, leading to a decrease in endolymphatic hydrops. The effect of stress reduction on patients with Menière's disease is frequently reported in the literature [17,18].

## **Conclusion**

Our patient group was found to be comparable to patient cohorts as reported in the literature with respect to gender distribution, age, duration and severity of the disease. The group can be regarded as representative with a high external validity. In this study

specific attention is paid to differences between affected and unaffected ears, as well as uni- and bilaterally affected patients. To our knowledge such specific analysis on these issues has not been reported in the literature.

In our population the duration of Menière's disease in bilaterally affected patients was longer than in unilaterally affected patients. This was probably not caused by a change-over from an unilateral start of the disease to a bilateral involvement of the disease. The ears of the bilaterally affected patient were both affected almost from the beginning of the disease, suggesting a bilaterality as a separate entity.

The severity of symptoms did not correlate with the duration of the disease. The fact that aural pressure/fullness had a high correlation with tinnitus indicates that this symptom is not obligatory for the definition of Menière's disease.

## References

- 1 Paparella MM, Griebie MS. Bilaterality of Menière's disease. *Acta Otolaryngol (Stockholm)* 1984;97(3-4):233-237.
- 2 Kodama A, Kitahara M, kitanishi T. Clinical findings in patients with bilateral fluctuant hearing loss. *Acta Otolaryngol* 1995;519:227229.
- 3 Watanabe Y, Mizukoshi K, Shojaku H, Watanabe I, Hinoki M, Kitahara M. Epidemiological and clinical characteristics of Menière's disease in Japan. *Act Otolaryngol (Stockholm)* 1995;519:206-210.
- 4 Pfaltz CR. Vestibular diagnosis in Menière's disease. *Arch Otorhinolaryngol* 1976;16:321-329.
- 5 Ralli G, Celestino D, Fabbricatore M, Lamberti A. Initial symptoms in Menière's disease. *Acta Otorhinolaryngol Ital* 1995;15(1):9-14.
- 6 Watanabe I. Menière's disease with special emphasis on epidemiology, diagnosis and prognosis. *ORL* 1980;42:20-45.
- 7 Gentine A. Contribution à l' étude de la maladie de Menière. Thèse Univ. Strassbourg 1975;79ff.
- 8 Balkany TJ, Sires B, Arenberg IK. Bilateral aspects of Menière's disease: an underestimated clinical entity. *Otolaryngol Clin North Am* 1980;13:603-609.
- 9 Friberg U, Stahle J, Svedberg A. The natural course of Menière's disease. *Otolaryngology (Stockholm)* 1984;406:72-77.
- 10 Morrison AW. Management of sensorineural deafness. Butterwords, London 1975;145-174.
- 11 Stahle J, Friberg U, Svedberg A. Long-term progression of Menière's disease. *Acta Otolaryngol* 1991;485:78-83.

- 12 Matsuoka I, Kurata K, Kazama N, Nakamura T, Sugimaru T, Satoh M. The beginning of Menière's disease. *Acta Otolaryngol* 1991;481 505- 509.
- 13 Silverstein H, Smouha E, Jones R. Natural history vs surgery for Menière's disease. *Otolaryngol Head and Neck Surg* 1989;100:6-16.
- 14 Filipo R, Barbara M. Natural history of Menière's disease: Staging the patients or their symptoms? *Acta Otolaryngol* 1997;526:10-13.
- 15 Committee on hearing and equilibrium guidelines for the diagnosis and evaluation of therapy in Menière's disease. Committee on hearing and equilibrium, *Otolaryngology-Head and Neck Surgery* 1995;113/3:181-185.
- 16 Yamakawa K. Pathologic change in a Menière's patient. *J Otolaryngol Jpn* 1938;44:2310-2.
- 17 Groen JJ, Schmidt PH. 'Psychosomatische aspecten van de ziekte van Menière' (in Dutch). Utrecht: Bohn, Scheltema en Holkema, 1984.
- 18 Savastano M, Maron MB, Mangialaio M, Longhi P, Rizzardo R. Illness behaviour, personal traits, anxiety, and depression in patients with Menière's disease. *J Otolaryngol* 1996;25:5:329-333.