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Hypertension and Diabetes Mellitus are Features of Vascular Dementia, Not Alzheimer's Disease

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Background

Alzheimer´s Disease (AD) is the most prevalent type of dementia/major cognitive disorder (40%-70% of cases) [1-4], still increasing in prevalence with the growing elderly population [5]. Over the past years, it has been proposed that Diabetes Mellitus (DM) [6,7] and Hypertension (HT) [6,8] are risk factors for AD. These are well known risk factors for vascular dementia (VaD) [9], which is a brain disorder where cerebrovascular pathologies are accountable for the cognitive impairment, without significant impact of other pathologies [9,10]. Thus, the pathogenesis of VaD is conceptually different from that of AD. The purpose of this study was to investigate the prevalence of DM and HT in AD, VaD and mixed AD-VaD (MD).

Material and Methods

Autopsy reports from the clinical department of Pathology in Lund from 1992-2017 were analysed. All cases with 1) A clinical diagnosis of dementia/cognitive disorder; 2) A complete autopsy report and 3) a neuropathologically confirmed diagnosis of AD, VaD or MD were included.

Clinical data regarding DM and HT were retrieved from the Swedish National Diabetes Register (NDR) and the medical records. The definition of HT was set, in accordance with contemporary guidelines, at a blood pressure of ≥140/90 [11]. All subjects with anti-hypertensive treatment were defined as having HT. Regarding DM, only presence or absences of diagnosis were considered.

The procedures of the brain investigation were made according to standard procedures in our laboratory [12]. In brief it included a detailed examination of the entire brain and lobar regions on small and whole-brain coronal sections. AD was defined as Braak stage III or more [13,14]. VaD was defined as clear vascular ischemic pathology without significant neurodegenerative changes [15]. MD was defined as significant AD pathology (at least Braak stage III) and concomitant significant vascular-ischemic pathology [16-19]. The three groups were compared using crosstabs and Pearson Chi-Square test to test for significance, followed by pair-wise comparisons and subsequent Bonferroni correction for multiple analyses. A p-value of 0.05 was considered statistically significant.

Results

A total of 268 subjects were included [18], the cohort of AD comprising 81 subjects (30%), the MD group comprising 81 (30%) and the VaD group holding 106 cases (40%). Data regarding DM and HT was not obtainable in all subjects, but for DM the mean proportion of obtainable data was 65% (62%-70%) of the subjects and for HT the mean of obtainable data was 74% (70%-76%) of the subjects.

DM (calculated from obtainable data) was reported in 12% of the AD group compared to 31% of the VaD group ($p<0.001$), and to 19% of the MD group (Figure 1). Hypertension was reported in 37% of the AD group compared to 74% of the VaD group ($p<0.001$). 44% of the MD group reported with HT (Figure 2).

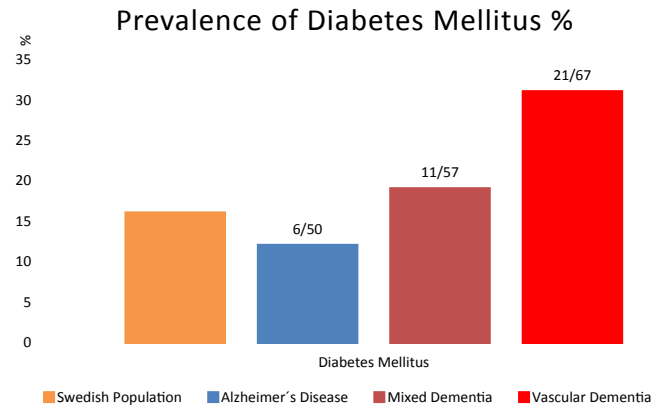

Figure 1: Prevalence of diabetes mellitus among the obtainable data in the different study groups (%).

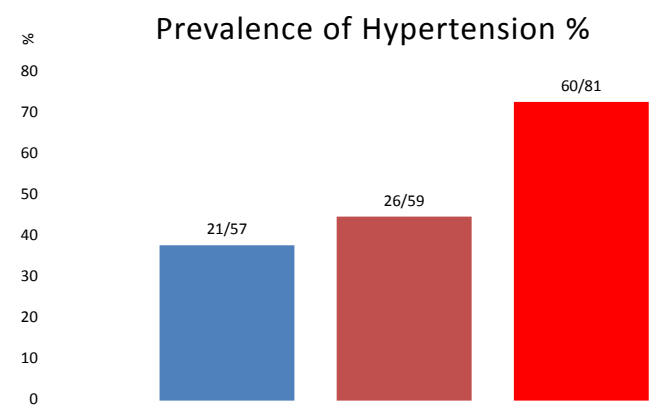

Figure 2: Prevalence of hypertension among the obtainable data in the different study groups (%).

Conclusion

In this study we found that the prevalence of both DM and HT is clearly different between AD and VaD, which is not surprising as they

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display markedly dissimilar pathologies. In both studied risk factors, MD exhibited prevalence in between that of AD and VaD.

Interestingly, and what could be interpreted as a strong indication that DM does not contribute to AD pathology, only 12% of our AD group had a diagnosis of DM, a frequency lower than what is reported in the general Swedish population (15,6%) in a similar age group, >65 years.

We believe that these findings stress the importance of telling AD and VaD apart, since it is fundamental to separate these two different entities for the assessment of risk factors, disease associations and possible treatment of two dissimilar diseases. This text is based on a published article in Journal of Alzheimer´s Disease from Javanshiri et al.

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