Highlighting the need for better care planning in young onset dementia

Commentary on 'Comparing survival and mortality in patients with late-onset and young-onset vascular dementia' by Yoo *et al*

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Young onset dementia (YOD) is widely accepted as dementia with onset below the age of 65 (van de Veen., 2022). People living with YOD have distinctive and wide-ranging needs due to age, life stage and the range of rare diagnoses. YOD is associated with delays in diagnosis, high socioeconomic impact (Kandiah *et al.,* 2016), increased carer burden (Lim *et al.*, 2018) and increased rate of neuropsychiatric symptoms (Van Vliet et al., 2013) compared to late onset (LO) dementia. The numerical dominance of LO dementia means that service provision for YOD remains highly variable, with poorly defined care pathways, lack of specialist services and limited access to targeted care planning and age-specific interventions that promote continuing capability and well-being (Carter *et al.*, 2018).

In order to inform the development of services and to provide clear information to young people and their families living with dementia, more data regarding the presentation and course of YOD is needed.

Currently, understanding of important areas of YOD is lacking, with the variability in reports of time to diagnosis being a prime example of this. A key study found that diagnosis in YOD takes twice as long as in late onset dementia (4.4 vs 2.8 years) (Van Vliet *et al*., 2013). Draper *et al.* (Draper *et al*.,2016) found a similarly prolonged journey to diagnosis, with a mean time to final diagnosis of specific dementia subtype of 4.7 years. Factors that may influence time to diagnosis include access to specialist services. In I*nternational Psychogeriatrics,* a 2022 study by *Loi et al*. (Loi *et al.*, 2022) demonstrated that access to a specialist multidisciplinary young onset dementia service may reduce time to diagnosis by 12 months. Stamou *et al*., (Stamou *et al*., 2021) reported that Individuals diagnosed in a specialist young onset dementia service compared to other settings, are more likely to receive support within the first six weeks and receive ongoing care in the service where they were diagnosed. Specialist young onset dementia services also performed better than other types of service on quality indicators, including providing care plans and key workers. These findings underscore the improved continuity, quality and satisfaction that can be delivered by specialist services.

In order to improve understanding of YOD and in order to plan appropriate specialist services that meet need, better insight into survival time and comorbid influences is necessary.

Consensus in the literature regarding survival varies. For example, a six-year cohort follow up study in individuals with young onset dementia in The Netherlands (Gerritsen *et al.,* 2019) identified that later age of onset of dementia was associated with reduced survival time after symptom onset and diagnosis. Individuals with young onset Alzheimer's disease had statistically significant shorter survival times compared to those with vascular dementia (VaD) (median 8.6 and 14.6 respectively). However, the authors were not able to account for the uncertainties derived from self-report about symptom onset, nor the possibility that people with YOD were over-represented in the 21% attrition due to their prolonged survival. Furthermore, a cohort control study of individuals diagnosed in a memory service using a death registry identified no difference in survival from diagnosis in YO vs LO dementia (Rhodius-Meester *et al.,*2019). A recent analysis of national dementia datasets in England demonstrated that 55.1% of those currently living with dementia aged between 65 and 69 years were diagnosed under the age of 65 (young onset). Of this age group, half have lived with dementia for 3 years or less, 25% for more than 5 years and 5% in excess of 12 years (Carter *et al.*, 2022).

Prior to the study by Yoo *et al*, (Yoo *et al*., 2023) in *International Psychogeriatrics* no specific data was available regarding the impact of age of onset on survival specifically in vascular dementia. This represents an important advance since vascular dementia (VaD) is a potential target for primary prevention, particularly in 'older onset' YOD (ages 45-65) where causes of dementia are less likely to be genetic.

In their retrospective case note review, Yoo *et al* investigated survival in people with young-onset VaD (YO-VaD, n=43) compared to those with late-onset VaD (LO-VaD, n=37) and predictors of mortality. The study reported that median survival for LO-VaD was 6.1 years and for YO-VaD 12.8 years. The only significant predictor of mortality was increasing age, with no effect found for the number of vascular risk factors, smoking status, hypertension or Hachinski score (Hachinski *et al*., 2012). Of note, VaD conferred a high risk of mortality compared to the general population; approximately 3× for LO-VaD and 6x for YO-VaD. With each year of advancing age, mortality risk increased by approximately 6%.

The key finding from this study is that younger people living with VaD have shorter life expectancy than age peers but live for longer with dementia than people with LO VaD. Whilst the study presents new data in the field of survival and mortality in YO VaD, some of the findings conflict with those from a detailed meta-analysis where cardiovascular risk factors and cardiovascular disease were associated with increased mortality in individuals with dementia (van Vorst *et al*., 2016). The authors recognise the limitations of the study including the specialist (tertiary neuropsychiatry inpatient) sample, retrospective design, use of neuroimaging reports rather than image analysis, and lack of information on severity of cerebrovascular disease or pathological diagnosis.

Perhaps the most significant impact from new studies on survival in young onset dementia for individuals, families and those working in the field, is the emerging data about length of time lived after diagnosis. As Yoo *et al* acknowledge, such contemporaneous information can help clinicians answer questions such as ‘ How long do I have? It also highlights that a diagnosis may present a relatively long time-frame to address changing needs, impact on carers and wider family and opportunities for holistic advanced care planning (Van Rickstal *et al*., 2023). All have implications for provision of appropriate service models in this cohort.

Questions remain about the relationship between vascular risk factors and vascular disease on survival and mortality in young onset dementia. In the Yoo *et al* study, no association was found between either Hachinski score or cardiovascular risk factors and survival in either YO or LO VaD.

Current efforts in the field to reduce risk of dementia is focused primarily on modifiable environmental risk factors and vascular risk factors such as hyperlipidaemias, obesity, smoking, diabetes and hypertension in midlife. Understanding risk factors for YOD, for example, how or if they differ from those for late onset disease and how they may vary with dementia subtype is important in informing efforts for prevention in non-genetic disease. Limited high-quality evidence from prospective longitudinal studies is available, but collective evidence is accruing about ‘critical windows’ in early and adult life that differentially affect risk of neurodegenerative disease and a dose response relationship for all-cause YOD depending on number and interaction with other exposures, across the life span (Cations et al, 2019). Recent commentary published in *International Psychogeriatrics* (Pini and Wennberg., 2022), for example, referenced a longitudinal follow up of a birth cohort (Krishna *et al.*, 2022) which found that greater size at birth was associated with better cognitive function in later live and this was partially mediated by childhood growth and environment. Of note, there was no evidence that midlife cardiometabolic factors mediated this association.

YOD is a clinically heterogeneous condition without the confounding effects of frailty. Risk factors applicable to older groups may or may not be generalisable. The data presented by Yoo *et al*, provides new evidence regarding survival and risk factors in a specific clinical cohort. The next, not insignificant, challenge remains extending such knowledge in epidemiological studies that consider risk over the life course of individuals and the differential effect of dementia subtype in well-defined cohorts without genetic risk.

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