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Hospitalisation and comorbidities in Parkinson's disease: A large Australian retrospect study

Michal Lubomski Dr.
6.0 CHAPTER 6 – DISCUSSION

6.1 Introduction

This chapter will present and evaluate the new information that was obtained from this investigation on hospitalised Parkinson’s disease patients in Australia. It will review the clinical significance of the results and reflect on the strengths and weaknesses of the study. It will address aspects of the study design and analysis, as well as consider the analytic and computational challenges encountered in the evaluation of comorbidities of Parkinson’s disease patients. Finally the implications of common adverse drug events for Parkinson’s disease patients are discussed and the association between DBS and hospitalisation is reviewed.

The results of this Master’s project provide insight into the importance of neuro-epidemiological research into Parkinson’s disease in Australia. This research gives new insights into the reasons for hospitalisation of patients, particularly with regards to the dramatically higher proportion of patients with Parkinson’s disease being hospitalised for delirium; adverse drug events; syncope; and falls/fractures compared to those from the comparison sample. Further, the burden of important comorbidities among Parkinson’s disease patients has also not been evaluated extensively, particularly in the Australian setting. Many of our study’s findings were novel and have not been previously described. The research described the important and clinically significant findings that were identified in the large dataset of Parkinson’s disease patients, which were informed by a review of the literature, and were compared to a reference population. This included important demographic features relating to length of stay, means of admission and separation, as well as comorbidities associated with the need for hospitalisation.

The conclusions drawn from the study could be used to inform the planning of health services by local and state health authorities, particularly emphasising the need for improved access to outpatient clinics to avoid unnecessary hospitalisations for the most frequent causes of Parkinson’s disease hospitalisation. Unfortunately there is a paucity of evidence that such
dedicated outpatient clinics currently minimise admission rates for patients with Parkinson's
disease within Australia. Accordingly, a follow on study could be beneficial to examine such
a hypothesis. Further, the results from our study could also be used to adjust current Activity
Based Funding for hospitalised Parkinson's disease patients. Finally, this study's findings
could be utilised to support financial provisions for services aiming to offer strategies to
minimise the length of stay of patients with Parkinson's disease.

6.2 Study Design

A descriptive analytic design based on a cross-sectional sample of patients with Parkinson's
disease and comparison sample of patients without Parkinson's disease was chosen to address
the aims of the study. The study was strengthened by the inclusion of admissions to all
hospitals (both public and private) in NSW over a number of years, making it large and
population-based. Of particular relevance was that the study considered patients who had
either a principal diagnosis or a comorbid diagnosis of Parkinson's disease (which is
important because a patient may have had an alternate major problem, such as a pneumonia
but the Parkinson's disease may have predisposed the patient to pneumonia). In addition, the
diagnoses used in this analysis were made by medical practitioners, rather than from than
from patient self-reports. This is likely to lead to a more accurate classification of patients
and is preferable to the methods used in other studies of Parkinson's disease. (62, 63)
Further, the study included a normative sample from the general patient population without
Parkinson's disease, which was selected using a random sampling technique and was
weighted according to the age distribution of patients with Parkinson's disease in the source
population.

However, there were a number of potential weaknesses in the study design. First, it is likely
that there were patients who were hospitalised and had Parkinson's disease but who were not
identified as having Parkinson's disease in the discharge summary and, therefore, were not
included in the study. The extent to which this occurred could not be determined in this
analysis and is, therefore, unknown. However, it is probable that this phenomenon is more
likely to be an issue for patients with milder disease rather than those with more severe

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Parkinson’s disease. In addition, it is possible that patients with a Parkinson’s disease diagnosis in the discharge summary may not have been coded as having Parkinson’s disease in the APDC or may have been miscoded as Parkinson’s disease but this is likely to be much less common than patients with Parkinson’s disease remaining unidentified by the clinicians managing the patient. This assumption is supported by the rigorous auditing procedures that are undertaken at both the hospital and departmental level in which the accuracy of coding of the diagnoses documented in the discharge summary is assessed. In addition, patients may have been included more than once in the dataset. This is because the records were not linked and individual patient histories could not be identified. This effect may vary depending on the severity of the patient’s illness, where the patients who had more severe illness may have had more frequent readmissions than patients whose disease was less severe. Patients may also have been excluded from the dataset if they sought treatment in alternate states/territories. This is particularly likely among patients living near state borders, and it is likely that the converse may also apply, whereby patients from nearby states/territories may have sought treatment in NSW. In this analysis, the in-hospital mortality rate was determined but it was not possible to estimate the number of deaths that occurred outside the hospital environment.

In this study, it was not possible to ascertain whether there was an under-recording or over-recording of a patient’s diagnosis as Parkinson’s disease, either as a primary diagnosis or co-morbidity, due to an error by the clinician or hospital coding staff. In addition, given the complexities of making a diagnosis of idiopathic Parkinson’s disease, it was not possible to verify its accuracy and it is possible that the accuracy varied between sites depending on the availability of specialist staff. This could be reflected in the possible under-reporting of the Parkinson’s disease hospital separations in this study, as these comprised only 0.04% of the admissions in our source population but there are estimates from other studies that the prevalence of Parkinson’s disease in Australia is higher, and was found to be 0.46% in the Blue Mountains Study, (53) and approximately 0.3% in an Access Economics Report. (21)

Activity Based Funding (and therefore, financial incentive for increased diagnoses) was introduced mid-way through the study period, and it is unknown whether this led to an increase in recording of Parkinson’s disease as a comorbidity in the APDC. In an attempt to verify true Parkinson’s diagnoses, we initially planned to assess medication lists, looking for
typical Parkinson’s disease medications such as L-dopa based treatments and dopaminergic agonists to validate a probable Parkinson’s disease diagnosis. Unfortunately, this data was not available from the Ministry of Health, thus this validation of the recorded diagnosis of Parkinson’s disease could not be conducted.

Other potential weaknesses in our study design were related to the selection of a suitable comparison sample group. This included the need to exclude certain types of hospitalisations (rehabilitation, psychiatric and dialysis services), given their varied length of stay, and types of treatment offered during such admissions. Regarding the normative population sample, various logistical issues existed within the Ministry of Health. In the database, public and private datasets are maintained separately, making it difficult to generate a sample group over the 5-year study period. Accordingly, a representative sample of patients from a single year, 2008, was used. The same exclusion criteria were applied to the comparison sample as the Parkinson’s disease sample, however is was apparent that a higher proportion of patients in the control group had shorter hospital stays, often one-day admissions for day procedure cases. This notion was supported by the difference in median LOS between the groups, 7 for Parkinson’s disease and 1 for the control group. We decided against imposing further exclusion criteria on the comparison sample (for instance, eliminating day procedures), we believe this would negatively impact on the generalizability of the results. We hope to address this problem more effectively in subsequent planned analyses, as discussed in Future Directions. One strategy would be to exclude all patients from both groups who were admitted for day procedures.

A potential bias within our study design could also result from the lack of homogeneity in the proportions of patients in our dataset, with regard to the proportions of public and private hospitalisations, as well as emergency and planned admissions. It is probable that such a variety of differing presentation types reflected differing models of care available to patients, resulting in potentially more unwell patients being managed through the public system and presenting through Emergency Departments and perhaps more elective/planned admissions resulting in slower stream medical/rehabilitation care being managed in the private system.
Approximately three-quarters of the Parkinson's disease patients in our study were admitted to private hospitals. It is plausible that there were different services available in the private and public sectors, including the availability of allied health interventions as well as procedures, such as DBS, which was overwhelmingly found in private hospital admissions. These differences may have impacted on outcomes such as LOS, as well as accounting for some differences in complications arising during admission, including delirium, adverse drug events, syncope and falls/fractures. A sub-group analysis of private versus public patients or emergency versus elective admissions could have been considered to further evaluate potential management differences, however it was considered outside the scope of the current project but could be considered in further analyses.

6.3 Study Analysis

A variety of statistical tests were performed in the analysis of our data with the aim of providing a clear understanding of the comparison between our Parkinson's disease patients and the comparison group. T-tests and chi-squared tests were used for comparison of continuous and nominal demographic and diagnosis related data respectively. The ability to demonstrate patterns in admissions in a substantial proportion of our data analysis through these tests was a significant strength to our data analysis.

There were however substantial differences in the distribution of the variable LOS between groups and for this reason a non-parametric test was utilised to assess the median difference in LOS, accompanied by interquartile ranges for comparison. Adjustment for multiple pairwise tests is undertaken in some studies and is a valid approach for dealing with multiple comparisons, however, this was not conducted in this analysis.

Logistic regression modelling was performed to explore the relationships between the groups of interest (patients with Parkinson's disease and the comparison group) and a series of dichotomous outcome variables. This is the appropriate choice of model in this situation and allows for estimations of effect after controlling for differences in demographic features and
comorbidities between the sample groups. The rationale employed in developing the logistic regression models aimed to demonstrate which of a number of observed bivariate associations was significant, after controlling for the associations of all variables in the model with the outcome of interest. This allowed for the control of demographic characteristics (including age, gender, marital status, hospital type and LOS) while assessing the effect of a predictor variable. Importantly, it was identified that encephalopathy/delirium, adverse drug events, falls/fractures, dementia, pneumonia, syncope/orthostatic hypotension, neoplasia and reduced mobility admission were significantly more common in the Parkinson’s disease population than in the comparison group, after controlling for the differences in demographic characteristics between the two samples. These findings from the logistic modeling strengthened our study’s comparative analysis.

6.4 Patient Comorbidities

An interesting observation from our study was the relationship between Parkinson’s disease and vascular disease co-morbidities, particularly relating to stroke and heart disease. We identified that our cohort of Parkinson’s disease patients had fewer admissions for ischemic heart disease / heart failure or arrhythmia than the control group, 16.7% versus 24.0%, but no difference in stroke hospitalizations (3.9% versus 4.0%). The exact reason for this observed effect is not entirely clear, as other worldwide studies have also suggested that cardiovascular disease rates were lower in patients with Parkinson’s disease. (14, 38) If, indeed, there was an overall difference between the Parkinson’s disease population and the control group in the prevalence of systemic vascular disease, then stroke rates would also be expected to be lower in the Parkinson’s disease than the comparison group. However this effect was not found.

One reason for the observed differences in ischemic heart disease admissions may be that there are lower smoking rates in Parkinson’s disease. (64) This assumption may be reinforced by the fact that there were significantly fewer admissions for chronic airways disease in the Parkinson’s disease than in the comparison group, 2.9% versus 7.2%. However it is probable that other confounders such as other lifestyle factors including exercise and diet, medications such as antihypertensives, lipid lowering treatment and control of diabetes could all have an
impact on this result. Unfortunately, these variables were not available in the dataset for analysis.

A final interesting difference in the distribution of comorbidities that we observed was the subgroup difference for melanoma hospital admissions. Previous studies, although controversial and of lower quality, have indicated that melanoma rates are slightly increased in the Parkinson’s disease population compared to the general population, and they have hypothesized that this may be related to levodopa use. (65) This notion was not reflected in our analysis, where 0.25% of the Parkinson’s disease hospitalizations compared with 0.51% of the comparison sample hospital admissions had a diagnosis of melanoma. This apparent difference could suggest that there was significant under reporting of melanoma comorbidities for Parkinson’s disease patients, or possibly that access to treatment for skin disease / skin cancer during a hospitalization may be different between Parkinson’s disease and control group patients. A plausible reason for the lower levels of hospitalization for melanoma among Parkinson’s disease patients could not be suggested outside of the usual sun-avoidance measures and patient infirmity.

6.5 Adverse Drug Events

An important finding of our analysis was that adverse drug events were significantly higher in the Parkinson’s disease population than the comparison group. This has important implications, given that many patients with Parkinson’s disease usually require a strict time-dependant administration of dopamine replacement medication to control their motor symptoms. Issues relating to incorrect administration / timing of patients’ regular medication, omission of doses or, importantly, drug interactions with other classes of medications, particularly dopamine blocking agents, can have profoundly adverse side effects. These can negatively influence Parkinson’s disease patients’ welfare and predispose them to increased complications that may lead to prolonged periods of hospitalisation. We found that the most frequent adverse drug events included: confusion, dystonic / extra pyramidal effects, postural hypotension, anticholinergic events, sedation and drowsiness and gastrointestinal disorders. It has been argued that perhaps an effective measure for reducing in-hospital medication related
side effects could be achieved by allowing selected patients to take control of the administration of their own Parkinson's disease medications. (66)

6.6 Deep Brain Stimulation And Its Effects On Hospitalisation.

There has been recent research on the effects of DBS in Parkinson's disease, with regard to the investigation of potential differences in modifying strategies to minimise adverse outcomes, differences in length of stay, and determination of the improvements in the quality of life of Parkinson's disease patients. (67, 68) With increasing numbers of patients gaining access to DBS across the world, more detailed studies are now available on the types of complications that arise from initial device implantation as well as the provision of follow up care. (69, 70)

A recent Portuguese study analysing long-term mortality in DBS in 184 patients, followed up patients for a mean of 50 months. It showed that 15 deaths occurred during the study, (total 8.15%, expected annual mortality rate 1.94%), (71) inferring that these rates were comparable or perhaps even lower than those receiving best medical therapy. (71-73) This may be a reflection of improved motor control leading to fewer complications such as falls and fractures in addition to increased medical surveillance of Parkinson's disease patients with DBS, prompting earlier consideration to changes in management. Further analysis of DBS patients showed that the most common causes of mortality included stroke, myocardial infarction, other vascular/heart disorders, or severe infection, with one suicide being recorded. (71) These patients' morbidities were quite similar to those identified in our study, however we were not able to discern the actual causes of death during hospitalisation due to lack of appropriate data-linkage. Overall it has been shown that DBS survival rates exceed 99% and 94% at 3 and 5 years respectively. (71, 72)

Further, an analysis of DBS Parkinson's disease cohorts across various centres within the United States of America suggest that patients with DBS may have improved healthcare outcomes in terms of minimized adverse events and complications as well as decreased
length of stay. (74) However, there were specific caveats noted within this study, with large volume, academic centres showing the most favourable results. Although the authors make recommendations supporting widespread availability of DBS across smaller, academic centres including those in rural areas, ultimately they highlight the importance of DBS providing easier access for patients to advanced Parkinson’s disease treatment, as well as reducing the total cost of hospitalisation. (74)

6.7 Conclusion

Planning and subsequently analysing this large population study was a challenging yet rewarding project. Learning to incorporate bio-statistical methodology such as the use of a robust comparator group, large population sample and comprehensive yet straightforward data analysis was intrinsic to the aim for the study that was published in a highly reputable peer reviewed journal. These features were planned from the initial phases of the study and were continually reviewed to make sure the project delivered on its objective to provide a clear understanding to the reasons for hospitalisations of Parkinson’s disease patients in NSW, as well as in-depth analysis of the comorbidities of hospitalised Parkinson’s disease patients.

Various complexities including the composition of the comparison group, management of multiple ICD diagnoses into workable diagnostic groups and others mentioned above needed to be continually refined to enhance the analysis of the results and allow for logical conclusions to be drawn from the results.