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

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2.0 Chapter 2 - Background

2.01 Introduction

Parkinson’s disease is a chronic, disabling and progressive neurological disorder of the basal ganglia within the central nervous system. This disease process results in a disruption of dopaminergic neurotransmission, leading to deregulated motor control, as a consequence of impaired feedback control mechanisms between various basal ganglia and the cerebral cortex. Histopathological examination demonstrates significant loss of dopaminergic neurons within the substantia nigra, with cytoplasmic inclusions (Lewy Body) deposition across cortical and subcortical structures. (1) This process leads to the ultimate development of extrapyramidal features, which are well recognised with Parkinson’s disease. These include involuntary movements, a rest tremor, cogwheel rigidity, and slowness in movement (bradykinesia). Cognitive impairment may also develop at a later stage as the disease progresses. (2)

Idiopathic Parkinson’s disease is the most prevalent form of the disease, affecting approximately 80% of all patients with Parkinsonian features. (3) The remaining patients manifest the parkinsonian phenotype as a consequence of a number of other causes. These include toxins, such as MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), infections of the central nervous system, structural lesions of the brain including ischemia, metabolic disorders and exposure to neuroleptic medication. (1) Aside from secondary parkinsonism due to medications and ischemia, most of these causes are rare and are often able to be differentiated by history, examination and neuroimaging.

Advancing age is the most common risk factor for developing Parkinson’s disease. However, there is an increasing body of evidence suggesting that genetic influences may have a role in the development of this disease, particularly if the age of onset is below 50 years. (4) Approximately 15% of people with Parkinson’s disease have an affected first degree or second-degree relative. (4) Other epidemiological studies suggest that male gender is associated with an increased risk of developing Parkinson’s disease, in addition to a an inverse relationship being observed with tobacco use and caffeine consumption. There are also indications that environmental factors (pesticide exposure), occupation, elevated blood
urate levels, NSAID use, and brain injury may also have a limited role in the development of this illness. (5)

Parkinson’s disease is a complex illness that manifests in a number of cardinal motor signs and symptoms, which include rest tremor, rigidity, bradykinesia, and postural instability. Common non-motor symptoms include anosmia, constipation, Rapid Eye Movement (REM) sleep behaviour disorder, depression and cognitive impairment. (1, 6) The symptoms experienced by patients can vary according to the age of onset, disease duration and severity. The levels of disability and impairment can be profound, especially in the latter stages of disease. Patients often require increased care as the disease progresses due to increasing levels of disability, which impede the ability to manage daily tasks, such as bathing, dressing and meal preparation. (7) Depression is a common problem and this may reduce a patient’s quality of life substantially. (8)

Standardised scores assist clinicians to assess aspects of the severity of the patient’s disease and disability. Motor scores are frequently assessed by UPDRS scale (Unified Parkinson’s Disease Rating Scale), with higher levels on this scale indicating more severe disease. (9) The Hoehn and Yahr Scale has been traditionally used to depict the stages of Parkinson’s disease relating to impairment or disability: 0 to 1 – mild disease, 2-3 moderate impairment and 4-5 severe disability. (10)

Early diagnosis and treatment of Parkinson’s disease can positively influence the patient’s experience of living with the disease and that of their family and carers. (11, 12) Misdiagnosis and delayed presentation contribute substantially to patient anxiety and diminished perceptions of self-efficacy in managing the illness and this, in turn, can reduce the patient’s quality of life. (12) In particular, older age, poor cognition and lower levels of mobility are determinants of sub-optimal outcomes for patients (13) Comorbidities also significantly influence the health outcomes of patients, particularly in the context of advancing age. (14) It has been shown that multiple medical system comorbidities occur frequently in people with mild to moderate Parkinson’s disease and advanced age, with
recommendations suggesting that early intervention, particularly screening for balance and gait impairment, is important to delay the development of mobility disability. (15)

A further important predictor of health related outcomes for patients with Parkinson’s disease is their access to a range of allied health services, which commonly include physiotherapy, occupational therapy, and speech therapy. In addition, some patients are benefitted by psychological interventions, as well as the provision of social support services. (14, 16-18) However, it has been demonstrated that patients with a higher number of comorbidities and advanced age are the least likely to benefit from access to these support services. (17, 18)

2.02 Incidence And Prevalence

In Australia, there are approximately 8,900 new cases of Parkinson’s disease each year and the illness is slightly more common in men than women. (19) The median life expectancy from disease onset to death is 12.2 years. (19) Due to the aging of the Australian population, the prevalence of people living with Parkinson’s disease is expected to increase substantially over time and it is estimated that by 2025 there will be approximately 98,500 people living with Parkinson’s disease, resulting in a greatly increased demand for health services. (19) Despite its prevalence, there is a paucity of information within Australia about the use of health services according to the age of the patient, or the duration or clinical severity of the illness.

Parkinson’s disease is the second most common neurological disorder in Australia and approximately 30 Australians are diagnosed with Parkinson’s disease every day. Parkinson’s disease affects patients in all age groups but is more common among older people, with a peak incidence in the early 60-year age group. It has an estimated prevalence of one percent after the age of 65 years. (20) However, Parkinson’s disease can also affect younger people, (typically less 50 years of age), with 20% of those affected being of working age. (21) This often places increased financial and social strains on younger families, which often include children. The incidence of Parkinson’s disease can vary between populations, with the highest prevalence being found in Caucasian populations. (22) In addition, there is some
evidence to suggest that Parkinson’s disease is more common in rural than metropolitan areas in Australia. (23)

2.03 Clinical Management

Although medical treatment with dopamine replacement is the primary management option for most patients with this disease, a variety of surgical and rehabilitation options have been shown to be of additional benefit. (24) Common surgical interventions for patients with predominantly motor fluctuations include Deep Brain Stimulation or various lesioning techniques, which are less commonly utilised in modern practice. (25) Rehabilitation goals can vary between patients, however therapy typically focuses on gait and balance, postural stability, as well as falls prevention. (26) Higher levels of impairment and increased restrictions due to progressive disease result in many Parkinson’s disease patients being referred to allied health services. These include speech therapy for swallowing and aspiration assessments; occupational therapy to assist with functional independence, including provisions of walking aids and modifiable home installations; and physical therapy to improve muscle strength and balance with the aim of minimising falls. (26) In addition, there is evidence to suggest that a multidisciplinary approach between the various health care providers can optimise health outcomes for patients. (16) However, for many patients, access to such services can be sporadic and uncoordinated, particularly across regional and remote areas. (27) Furthermore, access to health services, including allied health and psychological support services can vary between population sub-groups depending on their income and ability to afford private health insurance. (28, 29)

Patient comorbidities have a significant impact on the clinical management of Parkinson’s disease patients, both in the inpatient and outpatient setting. This is particularly evident in relation to the effects of polypharmacy to treat a variety of comorbidities that may, in turn, result in the deterioration of another condition, thus leading to more complicated management and a potential risk for subsequent hospitalisation. Common adverse drug reactions include: worsening of motor symptom control secondary to neuroleptic medications that are used in behavioural and hallucination management; postural hypotension secondary
to antihypertensives; and worsening bowel and bladder control, delirium and cardiac arrhythmias that may occur with advancing Parkinson’s disease and Levodopa use in combination with cholinesterase inhibitors that are used for the management of cognitive impairment. It is often necessary to adjust Parkinson’s disease patient medications in response to changes in the clinical situation, as well as to address interactions that may occur in relation to coexisting medical problems. (30-32)

2.04 Hospital Management Of Parkinson’s Disease

Hospital services play an important role in the management of Parkinson’s disease, especially when the symptoms of the disease are particularly intrusive. In Australia, in 2009-10, there were 3179 hospitalisations for Parkinson’s disease as a primary diagnosis nationally. (21) However, this is likely to be an underestimate, especially in relation to the identification of Parkinson’s disease as a secondary diagnosis, which may either remain undiagnosed or may not be recorded in the discharge summary.

Hospital admission may be a reflection of inadequate outpatient care, either due to an inability to access necessary services or due to compliance issues. Admission to hospital is also infrequently used to clarify a Parkinson’s disease diagnosis, using a levodopa challenge. Hospitalisation for Parkinson’s disease patients carries significant risks of complications, which may be related to, for example, adverse drug reactions, delirium and falls. These may be attributable to existing comorbidities or natural disease progression. Despite this, there is a paucity of information on the underlying reasons for admission to hospital among Australian patients with Parkinson’s disease. In addition, there is very little information on the distribution of co-morbidities of Parkinson’s disease patients who are admitted to hospital. (7, 19)

Although motor disturbances in Parkinson’s disease are believed to be a significant cause of Parkinson’s disease related admissions, other less defined causes are likely to influence hospitalisation, particularly non-motor complaints. Nationally it was estimated that in 2009-10, 2220 hospital admissions were recorded for accidental falls as well as 2138 admissions
for pneumonia in the context of Parkinson’s disease related complications. (21) This was predicted to cost at least an additional $76.6 million to the health system. (21) Further, information regarding the types of health services used by hospitalised Parkinson’s disease patients during their hospital stay is largely unavailable in an Australian hospital setting. (33)

Although it is recognized that Parkinson’s disease patients are admitted to hospital at higher rates than other groups and frequently have longer stays than the general population, (30) few formalised interventions have been implemented with the aim of reducing the need for hospitalisation or for minimising the incidence of inpatient related complications. (30, 34, 35) A systematic review of the limited global literature investigating the reasons for admission and the impacts of Parkinson’s disease complications during an inpatient stay, identified higher incidences of aspiration pneumonia, trauma (inclusive of fractures), psychosis and sepsis in Parkinson’s disease patients than among controls. (30) In addition, a recent systematic review from the Netherlands suggested that Parkinson’s disease patients have a hospital stay of between 2-14 days longer than controls, with 7 to 28% of Parkinson’s disease patients being admitted to hospital each year. (36)

2.05 Reasons For Admission

Admissions to hospital for patients with Parkinson’s disease may either be planned or due to an acute problem needing immediate hospital management. In Parkinson’s disease, the diagnosis may be the principal cause of admission (the disease that contributed most to the length of stay) or, alternatively, Parkinson’s disease may be a comorbidity that makes the management of the patient’s principal problem more complicated. Accordingly our study was designed to investigate differing types of admissions for Parkinson’s disease, either as a principal or a secondary diagnosis. This enabled the investigation of the patterns of comorbidities in hospitalised patients with Parkinson’s disease.

In one Australian study conducted in 2006, patients with a primary diagnosis of Parkinson’s disease presented with the following problems as reasons for admission: falls and fractures
(13%), pneumonia (12%), cardiac issues/syncope (16%) and gastrointestinal disorders (11%). A systematic review (30) of the four major worldwide studies investigating reasons for admission in patients with a diagnosis of Parkinson’s disease, identified motor complications, falls and fractures, as well as pneumonia, as being the most common factors that precipitated the need for hospitalisation. (33, 35, 37, 38) Fluctuating motor control is a known significant predictor of hospitalisation, with complications arising from the motor impairment being a causal factor for higher rates of inpatient admissions, (30) with approximately 15% of admissions requiring active management for the primary motor syndrome. (33)

Many challenging clinical features are encountered in managing the hospitalised Parkinsonian patient. Early recognition and management of these possible problems may optimise the potential benefits of an inpatient stay, along with decreasing hospitalisation-related complications. An overview of some of the important considerations that influence clinical decisions during hospitalisation of a Parkinson’s disease patient is given below.

2.06 General Principles

There are a number of general principles that guide the management of patients with Parkinson’s disease in hospital. First, an early and complete assessment of medications, dosages and specific dose schedules is regarded as being the key step in minimising medication errors in hospital, as many of the medications are time critical. (30) Further, in order to prevent serious sequelae, it is vital to give consideration to the life threatening, although rare, risk of Neuroleptic Malignant Syndrome (NMS) that can arise with the sudden discontinuation of medications. (31) Formal assessment of mobility with physiotherapy is encouraged, particularly for the assessment of falls risk and rehabilitation requirements. Guidelines currently under development encourage formal evaluation of swallowing by speech therapists, as the risk of aspiration is often underestimated. (39)
2.07 Infections

Patients with Parkinson’s disease are at a significant risk of developing aspiration pneumonia, as a result of difficulties with swallowing. A Chinese study has shown this to be the most commonly reported cause of inpatient death in Parkinson’s disease. (40) Measures including teaching chin down swallowing and the introduction of nasogastric feeding have been successfully employed to prevent aspiration pneumonia. Furthermore, infections secondary to reduced mobility such as cystitis and decubitus ulcers have been shown to precipitate delirium in Parkinson’s disease, thus early aggressive antibiotic treatment has been shown to decrease rates of encephalopathic complications in the context of hospitalisation and ambulatory care. (40-42)

2.08 Delirium

There are a myriad of potential factors that can predispose an inpatient with Parkinson’s disease to an increased risk of delirium. These include: an unfamiliar environment; infection; changes in medications; the effects of drugs and anaesthesia; and constipation and pain. (30) Commonly prescribed medications that are centrally active pose the highest risk of encephalopathy. These include pharmaceutical agents from the classes of: benzodiazapines, other anxiolytics, narcotics, hypnotics and antidepressants. Other drug related delirium effects may result from the use of anticholinergic drugs, some antiemetics and some antihypertensive medications. Pharmacological treatment of delirium in Parkinson’s disease necessitates the avoidance of typical neuroleptics due to their propensity to exacerbate motor dysfunction, including rigidity. International guidelines now stipulate the use of atypical neuroleptics such as quetiapine or clozapine, in the context of delirium or psychosis in Parkinson’s disease, as these have not been shown to cause motor dysfunction. (30, 35, 43)

2.09 Falls And Fractures

Falls and fractures are one of the most common reasons for hospital admission in patients with Parkinson’s disease, with estimates of their occurrence ranging between 13-24% of all
hospital admissions. (33, 35, 37) Hip fractures are known to occur commonly in the context of Parkinson’s disease. (44) Pneumonia and delirium are known precipitants of admissions for fractures, as well as being commonly encountered complications post operatively. (30) Unfortunately no guidelines have been published that direct the management of patients who suffer from hip fractures. Generally the approach is to institute measures that are aimed at falls prevention; treatment of low bone density, including bisphosphonates and Vitamin D; and the provision of physical assistance devices, including ambulatory aids, such as canes, walkers and wheelchairs. (30)

2.10 Hypotension / Syncope

Orthostatic hypotension, which is a common cause of syncope in patients with Parkinson’s disease, is mediated by disease related autonomic instability as well as by the effects of medication, particularly levodopa. (30) Indeed, it has been found that syncope is one of the leading causes of hospitalisation in Parkinson’s disease patients, occurring in approximately 11% of those requiring hospitalisation. (30) Measures aimed at correcting hypotension focus on reductions in anti-hypertensive medications, and ensuring appropriate fluid intake, with a possible increase in salt consumption. Further pharmacological measures include the addition of the mineralcorticoid, fludrocortisone, as well as arterial pro-contraction agents such as midodrine. (30)

2.11 Venous Thrombosis

Venous thromboembolism (VTE) is a serious complication that can arise in Parkinson’s disease, even during short hospital admissions. In Parkinson’s disease, pulmonary embolism has been identified as being the second most common cause of inpatient death. (45) Appropriate prophylactic anticoagulation for VTE along with mechanical measures have been recommended to prevent VTE related inpatient complications.
2.12 Psychiatric Issues

Aside from the inpatient treatment for psychosis or delirium, as previously discussed, depression and anxiety are common psychiatric syndromes that require careful supportive management, often by pharmacological means. Treatment of depression with low dose tricyclic antidepressants (TCAs), as well as selective serotonin reuptake inhibitors (SSRIs), have been shown to significantly improve outcomes while offering minimal adverse effects. (46, 47) Refractory or medication resistant depression has been successfully treated with electroconvulsive therapy (ECT), where additional benefits in motor improvement lasting several weeks have also been observed. (47-49) Anxiety in Parkinson’s disease frequently presents with shortness of breath (30) or with concern about the medication “wearing off” phenomenon. (50) Benzodiazepines have been suggested as effective treatments for anxiety in this situation, however these medications predispose patients to an increased risk of falls, somnolence and confusion. Thus their use in anxiety should be carefully considered.

2.13 Elective Hospitalisation And Parkinson’s Disease

There is wide international variation in the reported numbers of elective admissions for patients with Parkinson’s disease. (51) A recent Italian study suggested that as many as 20% of Parkinson’s disease hospitalisations were planned. Commonly occurring planned admissions included musculoskeletal ailments, rehabilitation and cardiovascular disease management (52) In other studies, the reasons for elective admission included: elective surgery, rehabilitation, and medication management including drug holidays. (30) Tertiary centres report Deep Brain Stimulation (DBS) as the most common cause of elective hospitalisation in Parkinson’s disease. (30) Reports of elective surgery in patients with Parkinson’s disease have identified longer hospital stays, higher in-hospital mortality, as well as increased post-operative complication rates compared to controls. (34) However, early neurologic consultations for elective orthopaedic surgery have been shown to result in improved surgical outcomes and a reduced length of stay. (53)
2.14 Elective Surgery

Elective surgery predisposes a patient with Parkinson’s disease to an increased risk of delirium. Appropriate education and discussion of this risk with the patient and family may reduce the need for unnecessary post-operative investigations for causes of delirium should this occur. (30) Daily review and rational balancing between adequate analgesia and delirium risk has been recommended as good practice for Parkinson’s disease surgical patients. (30) Post operative complications due to gastric stasis pose challenges to ongoing medication administration, as there are no approved parenteral formulations for use in Parkinson’s disease. Recently however a dopamine agonist transdermal patch (Rotigotine) has been shown to be beneficial in the perioperative setting for management of Parkinson’s disease patients who are unable to receive oral medication. (54) Gastric stasis can result in an acute dopamine medication discontinuation, predisposing patients to the rare but serious effect of Neuroleptic Malignant Syndrome. (30) Suggested measures to avoid disruptions with time critical medication administration in Parkinson’s disease may include the alternative use of a dopamine agonist patch (Rotigotine), apomorphine subcutaneous infusions or the temporary insertion of a nasogastric tube for medication administration. (30)

2.15 Keeping Parkinson’s Disease Patients Out Of Hospital

Improved access to urgent outpatient Neurology Clinics has been shown to significantly reduce inpatient Parkinson’s disease hospitalisations according to a recent Israeli study. (35) This study identified that keeping an ‘open door policy’ to urgent outpatient Neurology Clinics was a successful means of reducing 50% of yearly admissions, as well as reducing the overall length of stay by 4 days. (35) Further, outpatient liaison, with ongoing input from speech therapy, occupational therapy, physiotherapy as well as neuropsychology, has also been shown to decrease the need for hospitalisation. (30)
2.16 Causes Of Death In Parkinson’s Disease

A recent review of deaths due to Parkinson’s disease in Australia showed that in 2011, 1692 people died due to the disease with very little information available about the exact causes of death. (21) With the predicted aging of the Australian population over the coming decades, these projections are expected to rise sharply, placing extra strain on hospitals, nursing homes, and the community to provide supportive services for people with late stage Parkinson’s disease. (21) Early international studies have identified that respiratory infections were the most common cause of out and inpatient Parkinson’s disease deaths. (55) Autonomic dysregulation was suggested as a potential causative mechanism in these deaths. (55) More recently, in a British study, pneumonia was documented as the terminal event in 45% of the deceased Parkinson’s disease patients. (56) In another review of common causes of death documented in death certificates identified: malignancy, ischemic heart disease, cerebrovascular disease, chronic lung disease, heart failure and dementia. (57) Interestingly death from malignancy and ischemic heart disease was lower in Parkinson’s disease patients than in controls. (56) However significant limitations in the documentation of the cause of death were commonly identified, with estimates of inadequate information in approximately one third of death certificates. (56)

A Canadian analysis identified that pulmonary embolism was the second most common cause of death, after respiratory infections, on autopsy examinations. (45) These authors suggested that other estimates of the causes of Parkinson’s disease deaths may have been misleading due to a lack of pathological / autopsy information. (45) Overall, estimates suggest that persons with Parkinson’s disease are at a 43% greater risk of all-cause mortality. Importantly, these patients have a 51% greater risk of injury-related mortality compared with the general population. (58) There is, however, a paucity of information about the causes of inpatient Parkinson’s disease deaths in Australia.
2.2 Discussion

The literature review presented in the preceding paragraphs describes the current knowledge of the role of hospitalisation in the management of Parkinson’s disease; the best measures to optimise care of these patients; and the impact of comorbidities on patient outcomes. However, knowledge about the reasons underlying admission among patients with either a principal or secondary diagnosis of Parkinson’s disease, as well as the effect of comorbidities on hospitalisation in Parkinson’s disease is incomplete.

This research project aims to address this deficiency in the international literature. First, it aims to describe the associations between demographic characteristics and comorbidities of Parkinson’s disease patients who have received hospital care and important health-related outcomes. Second, it aims to provide some information on service delivery to patients, including variations in access to advanced Parkinson’s disease therapies, including DBS. This research will add to the international literature by providing a large state-wide population analysis of Parkinson’s disease hospitalisations. By doing this, it is hoped that it will inform the tailoring of better service provision to patients with Parkinson’s disease.