

Parkinson's disease, deterioration during hospitalization

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Parkinson's disease

deterioration during hospitalization

Oliver Gerlach



Parkinson's disease, deterioration during hospitalization

Oliver Henricus Hubertus Gerlach

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Parkinson's disease, deterioration during hospitalization

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Universiteit Maastricht,
op gezag van de Rector Magnificus, Prof. dr. L.L.G. Soete,
volgens het besluit van het College van Decanen,
in het openbaar te verdedigen
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door

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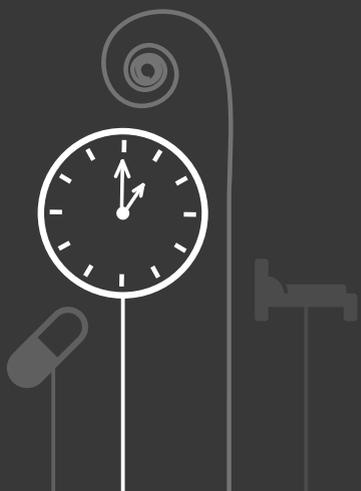
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A minimalist illustration on a dark background. On the left, a white clock face with two hands is mounted on a thin vertical stand. To its left, a grey pill is shown on a similar stand. To the right of the clock, a grey microscope is mounted on a stand. A decorative swirl is at the top of the clock's stand.

Chapter 1

GENERAL INTRODUCTION

GENERAL BACKGROUND OF PARKINSON'S DISEASE

Epidemiology

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease and one of the most common movement disorders.^{1,2,3}

The overall prevalence of PD is 1.4%. Prevalence increases with age; for those between 55 and 64 years, it is 0.4%, and 4.3% for those aged above 85 years.⁴

According to the general practitioners' registration system, there were almost 29,000 patients diagnosed with Parkinsonism, including Parkinson's disease, in the Netherlands in 2011.

Males are more frequently affected than females, i.e. 2.01 and 1.47 per 1000 respectively.⁵

It is likely that the total number of patients with Parkinsonism in general population will be 2 to 2.5 times higher because of under-registration.⁵ Because of demographic trends in Western countries, the prevalence may increase at 76% for men and 44% for women till the year 2030, due to aging and growth of our population.⁵

Pathogenesis

PD is characterized by progressive loss of dopamine producing neurons in mainly the substantia nigra in association with the presence of Lewy bodies in surviving neurons.^{3,6} The pathology is, however, more widespread than this specific area and neural system, involving

many areas of the brain, including the midbrain and neocortex and even other organs.^{7,8,9}

Despite much research as to the pathogenesis of PD, the exact cause is still unknown.^{1,3,10}

Different processes such as autophagy, mitochondrial and lysosomal dysfunction, inflammation, and protein mishandling may contribute to the disease.^{1,10} Although several causative genes have been discovered, the vast majority of the patients seem to have sporadic PD.^{1,3,11}

Next to this, there are both nonmodifiable (as age and gender) and modifiable environmental factors (as smoking and coffee consumption) that may influence the disease process.^{1,11}

Diagnosis

PD is a clinical diagnosis, as there are no biological markers or radiological findings during life that prove the diagnosis.^{3,8} Differentiating this hypokinetic-rigid syndrome from other Parkinsonian syndromes can be difficult.¹² The correct diagnosis can be confirmed only after death by postmortem pathological research.⁸

According to the UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria, the patient should have bradykinesia and at least one of the following: muscular rigidity, rest tremor (4-6Hz), and/or postural instability not caused by primary visual, vestibular, or proprioceptive dysfunction.⁸ Supportive for the diagnosis are unilateral onset, presence of rest tremor, progressive course, persisting asymmetry, excellent response to levodopa treatment, severe levodopa-induced chorea, levodopa response for at least 5 years, and a clinical course of more than 10 years.⁸

Symptoms

Motor symptoms

Motor symptoms, which develop gradually and can manifest themselves in a wide clinical spectrum, are the best known symptom of PD.^{13,14} The cardinal symptoms are slowness and poverty of movement, shaking, stiffness, and postural instability.^{12,14} Bradykinesia is essential for the diagnosis and can be both distally and axially located in the PD patient.^{8,13} Although asymmetric rest tremor is the most common initial symptom, tremor can be postural or mixed.^{13,15} Where dystonia can be one of the first symptoms of PD, postural balance problems are more common in advanced PD. PD patients often have gait problems. Initial gait disorders probably represent axial bradykinesia. More advanced PD patients can have freezing of gait which is often associated with the loss of postural reflexes. With progression of the disease, patients can also develop bulbar symptoms with dysarthria, hypophonia, and dysphagia.¹³

Non-motor symptoms

In literature, the focus has been mainly on motor symptoms and in daily practice, physicians fail to recognize non-motor symptoms.¹⁶⁻¹⁸ Non-motor symptoms, however, have gained considerable interest in recent years since increasing evidence demonstrates that these symptoms contribute to severe disability and impaired quality of life.^{17,18} The non-motor symptoms are very diverse.^{12,17,18} Non-motor symptoms as olfactory problems, constipation, depression, and rapid eye movement disorder can occur early in the disease.¹⁷ With progression of the disease, non-motor symptoms become more prominent and dominate the clinical picture.^{17,18} There are high rates of dementia in advanced PD, and many patients have cognitive impairment.^{17,19,20} Other mental health problems are depression, psychosis, anxiety, and apathy.^{12,16,17} Autonomic disturbances as postural hypotension, constipation, urological problems, hyperhidrosis, hypersalivation, and sexual dysfunction also have a great impact on daily living.^{12,17,21-23} Pain is common in PD patients.²⁴ Pain can be the result of both primary (e.g. as a result of dystonia) and secondary causes (e.g. due to musculoskeletal problems).^{12,17,24} Furthermore, sleep disturbances are widely present in PD patients, as is fatigue.^{12,16,17,25,26}

Treatment

Although there are no therapies that cure PD, there are a number of available symptomatic treatment options.^{12,27-30} Most patients get medical treatment. Dopaminergic medications as substitute for dopamine deficiency in the brain are one of the oldest and still most prescribed drugs for symptomatic treatment of PD. Levodopa is the most effective one, followed by dopamine receptor agonists.^{12,27-31} Monoamino-oxidase-B inhibitors can also be effective as mono therapy since it improves levels of dopamine by slowing the breakdown of dopamine in the brain. By adding catechol-O-methyltransferase inhibitors, on phases can be prolonged as it increases the level of peripheral plasmatic levodopa.^{12,27-30} Other

examples of oral medication that can reduce the severity of PD symptoms are amantadine, anticholinergics, beta-blockers, and clozapine.^{12,27,29}

In more advanced PD, there are more invasive therapeutic options. Pump therapies, e.g. apomorphine pump or parenteral levodopa/carbidopa intestinal gel pump provide a more continuous administration of drugs, which is more true to nature and therefore achieve a better therapeutic effect with less motor fluctuations.^{12,27,29,30}

In addition, neurosurgical interventions, i.e. high frequency deep brain stimulation or lesioning of specific brain areas can be considered when drug therapy is insufficient. Both the subthalamic nucleus and globus pallidus internus are the most commonly targeted sites.^{12,28,29,32-35}

All these therapeutic options can be effective in reducing motor symptoms. Treatment of non-motor symptoms and side effects of treatment, on the other hand, can be challenging and may require specific medication or nonpharmacological interventions.^{12,27-29,34,35}

Additionally, PD patients can benefit from rehabilitation, physical therapy, speech therapy, and occupational therapy.^{27,28,36-38}

Quality of life

Because of both motor and non-motor symptoms, PD is a complex disease.¹² Although there are positive effects of medical and non-medical treatment options, these interventions can have side effects.^{35,39} All these different aspects can have influence on quality of life of PD patients.³⁹⁻⁴² PD is one of the diseases having the highest impact on quality of life.⁴³ Non-motor symptoms, especially depression, are the greatest contributors to reduced quality of life, and with progression of the disease, the impact becomes more prominent.⁴⁰⁻⁴²

HEALTHCARE UTILIZATION

General

PD patients have high use of healthcare facilities, which is higher than age and sex matched controls.^{44,45} The use of a wide range of services results in a high level of direct (e.g. neurologists, general practitioner, (pharmaceutical) therapies, social workers, hospitalization, nursing home care) and indirect costs (e.g. informal care, productivity loss).⁴⁶⁻⁴⁹ In 2007, in the Netherlands total healthcare costs were 74.4 billion euro, with more costs per person with higher age.⁴⁵ Since the number of patients diagnosed with PD is expected to rise as the population ages, total costs will grow substantially over the next decades and the disease will create a considerable burden for patients and society.^{45,47,48}

Hospitalization

General

In 2010 in the Netherlands, there were almost 1,500 hospital admissions for patients with Parkinsonism, including Parkinson's disease (excluding daycare admissions), with average hospitalization duration of 12.6 days.⁵¹ A quarter of total healthcare costs are hospital related.⁵⁰ Patients with Parkinsonism (including Parkinson's disease) cost 267 million euro. Of Parkinsonism related costs, 8.5% was due to hospital care.⁵¹

Problems

Because of different aspects of PD, i.e. motor and non-motor symptoms, combined with comorbidities related to the average age of PD patients, there is a high risk of hospitalization, and the chances of adverse events during these admissions of this vulnerable patient group are considerable.

In general, adverse events are defined as injuries that were caused by medical management, rather than the underlying disease, resulting in prolonged hospitalization and/or disability.⁵²⁻⁵⁴ These events can result in injury varying from temporary disability to death.^{52,53} Most events cause temporary, minimal impairment.⁵³ These events are not uncommon in hospitals, and they occur in about 3-17% of the hospitalizations.^{52,54} The most common overall adverse events are complications from drugs, e.g. marrow depression, bleeding, complications of the central nervous system, and allergic reactions.⁵³ For patients undergoing surgery, wound infections are the most common type.⁵³ However, most of the adverse events aren't preventable or due to negligence care.^{52,53,55} Apart from the individual discomfort and distress adverse events cause the patient and/or family, the economic impact because of direct and indirect medical costs on the society is huge.^{56,57} For the Netherlands, the preventable direct medical costs are an estimated 1% of the national healthcare budget mainly because of longer hospitalizations.⁵⁶

In daily practice at the outpatient clinic, many PD patients report problems during hospital admission. Complications, medication errors and deterioration of motor function are examples of these encountered problems.⁵⁸⁻⁶⁰ These issues have not been studied systematically. Therefore, in this thesis, the hospitalized PD patient is the point of focus.

AIM AND OUTLINE OF THE THESIS

In the present study, we aimed to further investigate the spectrum of problems patients with PD encounter during these hospitalizations. We will analyze possible deterioration of Parkinson symptoms during hospital stay and its related risk factors to explore those aspects that can be changed to improve quality of care.

Therefore, in **Chapter 2**, we review the literature to investigate what is known about hospital admissions of PD patients and the extent of problems these patients have during their hospitalization. Also, related, possible solutions are explored. In **Chapter 3**, we retrospectively assess prevalence and risk factors of motor function deterioration in hospitalized PD patients. Subsequently, in **Chapter 4**, we explore the severity of motor function deterioration and its risk factors prospectively. **Chapter 5** presents the results of a prospective study analyzing prevalence of cognitive decline in PD patients and its possible risk factors during hospital stay. **Chapter 6** shows the results of a questionnaire examining if in daily practice, PD patients receive extra attention during hospital admission because of their vulnerability. Finally, in **Chapter 7**, the most important findings of this thesis are reflected and the directions for improvement of care and further research are outlined.

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CHAPTER 2

CLINICAL PROBLEMS IN THE HOSPITALIZED PARKINSON'S DISEASE PATIENT: SYSTEMATIC REVIEW

O.H.H. Gerlach, A.Winogrodzka, W.E.J. Weber.

Movement Disorders 2011;26:197-208.

ABSTRACT

Introduction

The clinical problems Parkinson's disease (PD) patients encounter when admitted to a hospital, are known to be numerous and serious.

Methods

These problems have been inventoried through a systematic review of literature on reasons for emergency and hospital admissions in PD patients, problems encountered during hospitalization, and possible solutions for the encountered problems using the Pubmed database.

Results

Most studies were retrospective on small numbers of patients. PD patients are hospitalized in frequencies ranging from 7 to 28% per year. PD/parkinsonism patients are approximately one and a half times more frequently and generally 2 to 14 days longer hospitalized than non-PD patients. Acute events occurring during hospitalization were mainly urinary infection, confusion, and pressure ulcers. Medication errors were also frequent adverse events. During and after surgery PD patients had an increased incidence of infections, confusion, falls, and decubitus, and 31% of patients was dissatisfied in the way their PD was managed. There are only two studies on medication continuation during surgery and one analyzing the effect of an early postoperative neurologic consultation, and numerous case reports, and opinionated views and reviews including other substitutes for dopaminergic medication intraoperatively.

Conclusions

The major clinical problems are injuries, infections, poor control of PD and complications of PD treatment. There are many (un-researched) proposals for improvement. A substantial number of PD patients' admissions might be prevented. There should be guidelines concerning the hospitalized PD patients, with accent on early neurological consultation and team work between different specialities, and incorporating non-oral dopaminergic replacement therapy when necessary.

INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disorder with a life-time risk of 2% in males and 1.3% in females.¹ Although the disorder is generally slowly progressive, it does have a major impact on disability and quality of life of affected patients.^{2,3} One of the lesser studied aspects of PD is the spectrum of problems PD patients encounter, once they are admitted to a hospital. In our own and others' experience hospital admissions of PD patients are often problematic, especially so when patients are admitted on non-neurological wards.^{4,5} Problem areas are exact timing or lack of drug administration, administration of contra-indicated drugs, complications due to immobilization, and psychiatric disorders triggered by the hospital admission.⁶⁻⁸ As most non-neurologically educated health care personnel are unfamiliar with PD, protocols would be helpful to improve the care of PD patients in such environments.

We recently surveyed the majority of movement disorder specialist neurologists in the Netherlands and found that no specific guidelines or protocols exist to guide caregivers and PD patients in the hospital environment. Before such guidelines can be formulated, one needs to know the prevalence and spectrum of the problems PD patients may experience during their hospital stay. To this end we systemically reviewed all the existing literature on the problems encountered by the hospitalized PD patients.

METHODS

We systematically reviewed the literature on reasons for emergency room (ER) and hospital admissions in patients with PD, problems encountered during hospitalization of this patient population, and possible solutions for the encountered problems, using the Pubmed database. Last research date was 17 June 2010.

To identify articles we included (combinations of) keywords: See Table 1 for search details.

Subsequently we analyzed the abstracts for relevant articles: as relevant articles we defined those as pertaining to the following four areas:

1. Analysis of prevalence and reasons for ER visits and subsequent admission.
2. Clinical problems during hospital stay.
3. Peri- and postoperative problems.
4. Suggestions for improvement of care for the hospitalized PD patient.

We also searched the reference list of each relevant article for other applicable articles.

In our search there were no language limitations. We excluded articles concerning brain surgery.

Table 1. Pubmed search details

Search	Number of hits
Parkinson* AND emergenc*	422
Parkinson* AND hospitali*	645
Parkinson* AND healthcare	892
Parkinson* AND hospital admission*	45
Parkinson* AND hospital utilization*	4
Parkinson* AND resource use	186
Parkinson* AND perioperative	93
Parkinson* AND preoperative	451
Parkinson* AND intraoperative	453
Parkinson* AND anesthes*	373
Parkinson* AND surgery AND cognit*	456
Parkinson* AND surgical problems	260
Parkinson* AND surgery AND apomorphine	289
Parkinson* AND postoperative	1231
Parkinson* AND surgery AND complication*	2241
Medication interruption OR drug manipulations OR discontinuation OR dose reduction AND levodopa	576
Parkinson* AND Drug withdrawal	607
Parkinson* AND lisuride	268
Parkinson* AND medication error	59
Amantadine AND intravenous*	106
Rotigotine	247
Parkinson* AND fracture	236
Parkinson* AND nurse	276
Parkinson* AND nurse specialist	26
Parkinson* AND orthopaedic	94
Parkinson* AND orthopedic*	52

RESULTS

Emergency room and hospital admissions

Patients with PD often need emergency treatment. There are 4 studies analyzing the reasons for ER admission^{4,9-11}, including one case report¹¹ (totalling 327 PD patients, Table 2). 16-45%

of PD patients visit an ER once a year.^{9,10,12,13} PD patients visit the ER more frequently than their matched reference group (0.6 versus 0.4; p=0.05).¹⁴

We found 12 studies on hospital admissions (Table 3): 11 studies totalling 3216 PD/parkinsonism patients^{4,9,10,13,15-19,21,22} and one study²⁰ on a database with 15304 PD/parkinsonism patients. In these studies PD patients are hospitalized in frequencies ranging from 7 – 28% per year.^{9,10,15,19,20}

PD/parkinsonism patients are hospitalized approximately one and a half times more frequently^{20,23,24} and generally 2 to 14 days longer^{12,16,17,19,21,24-29} than non-PD patients, although there is not a difference in every study.^{15,30}

Reasons for emergency and hospital admission can be divided in:

1. Direct disease related morbidity: motor complications, psychiatric symptoms, autonomic dysfunction, sensory symptoms, sleep disorders, and side effects of anti-parkinsonian drugs.
2. Indirect disease related morbidity: traumas and pneumonia.
3. Non-PD related causes.

As most studies vary greatly in selection of patients, exact relative proportions of these 3 groups cannot be assessed (Tables 2 and 3). Some studies found that PD patients are more likely to be admitted to the ER and hospital for complications of the disease and its management than for primary motor problems.^{13,18} A part (5-21%) of the patients were first diagnosed to have PD during a hospitalization.^{19,21}

Table 2. Emergency room admissions

Study	Inclusion	Exclusion	Number of patients	Design	Control group	ER admissions (%)	Reasons ER visit
Vargas 2007 ⁹	PD	- Hoehn &Yahr Stage 5 - Parkinsonism - Severe cognitive dysfunction	144	R	No	22% in 1 year	Primarily side effects of anti-Parkinsonian drugs
Cosentino 2005 ¹⁰	PD	- Parkinsonism - Admissions related to PD	130	R	No	22% in 1 year	- Injuries 61%, mainly fractures 37% - Abdominal pain 6% - Pneumonia, dysphagia, dyskinesia, epistaxis, hearing loss, pulp disease, teeth extraction, lumbago, pain in joint: all 3%
Martignoni 2004 ⁴	PD	- Parkinsonism	48	P	No	All selected patients	- Cardiovascular 27% - Trauma with fractures 19% - Chest or abdominal problems 19% - Neurological (both related and unrelated to PD) 17% - Head injury 6% - Hip prothesis displacement 2%
Factor 2000 ¹¹	PD		5	C	No	All selected patients	Severe motor off periods, dyskinesia, psychosis, acute confusion, panic disorder, pain

Abbreviations: PD: Parkinson’s disease, ER: emergency room, R: retrospective, P: prospective, C: case report.

Table 3. Hospital admissions

Study	Inclusion	Exclusion	Number	Design	Control group ^a	Hospital admissions	Five most frequent admission reasons admission
Vossius 2010 ¹⁵	PD		108 patients	P	Yes	All selected patients	<ul style="list-style-type: none"> - PD related symptoms 25% - Vascular disorders 14%: significant less than control group - Pulmonary disorders including pneumonia 12% - Trauma 12%: significant more than control group - Cancer 7%: significant less than control group <p><i>Remark: discharge diagnosis instead of admission diagnosis</i></p>
Klein 2009 ¹⁶	- PD -Emergency admissions to Neurological Department		143 patients	R	No	All selected patients	<ul style="list-style-type: none"> - Motor complications 37% - Psychosis 24% - Somatic problems 14%
Guneyssel 2008 ¹³	- PD - Emergency hospital admission	- Admissions resulting in death - PD diagnosis during ER visit	76 patients	P	No	All selected patients	<ul style="list-style-type: none"> - Trauma 28% - UTI 20% - Cardiovascular 15% - Pneumonia, cerebrovascular both 12% - GI 8%
Vargas 2007 ⁹	PD	- Hoehn &Yahr stage 5 - Parkinsonism - Severe cognitive dysfunction	144 patients	R	No	28% programmed admissions in 1 year	<ul style="list-style-type: none"> - Complication treatment - Drug adjustment
Louis 2007 ¹⁷	- Young-onset PD - 18-40 years old	Obstetrical admissions Patients with diagnosis paranoia or schizophrenia	714 patients	R	Yes	All selected patients	<ul style="list-style-type: none"> - Psychosis 23%: significant more than control group - Craniotomy 7%: significant more than control group - Pneumonia, UTI both 6% - Headache or seizure 4% - Rehabilitation 3%: significant more than control group <p><i>Remark: discharge diagnosis instead of admission diagnosis</i></p>
Temlett 2006 ¹⁸	PD		761 hospital admissions	R	No	All selected patients	<ul style="list-style-type: none"> - Primary for PD 15% - Falls and fractures 11% - Pneumonia, cardiac disease both 10% - GI 9% - Organic brain syndrome 6%
Cosentino 2005 ¹⁰	PD	- Parkinsonism - Admissions related to PD	130 patients	R	No	19% in 1 year	<ul style="list-style-type: none"> - Diseases of digestive system 17% - Diseases of circulatory system, rehabilitation both 14% - Cataract 10% - Injury, chest pain both 7%

							- Sleep disturbance, epistaxis, abdominal pain, osteoarthritis: all 3%
Woodford 2005 ¹⁹	- PD - Emergency hospital admission	- Parkinsonism - Elective admissions - Day-case procedures - Admissions resulting in death of patient	367 patients	R	No	35% in 4 year	- Cardiovascular 20% - Falls 13% - Pneumonia 11% - UTI 9% - Decreased mobility/ dyskinesia, psychiatric both 8%
Guttman 2004 ²⁰	- PD - Use of PD drugs	- < 25 years of age	15304 patients	R	Yes	68% in 6 years	<i>Compared with controls:</i> First: aspiration pneumonia Second: affective psychosis Third: hip fractures Fourth: urinary tract disorders including infections Fifth: septicemia
Martignoni 2004 ⁴	PD	Parkinsonism	132 patients	P	No	All selected patients	<i>Admission to neurological department:</i> - Poor control of PD symptoms 37% - Neurological 25% - Diagnosis confirmation, psychiatric complaints both 13% - Sudden worsening of motor symptoms 7% - Head trauma and fracture 2% <i>Admission to non-neurological department:</i> - Medical and infectious illnesses 27% - Traumas with fracture 24% - Cardio-circulatory 22%
Tan 1998 ²¹	PD	- Drug induced parkinsonism - Parkinson-plus syndromes	173 patients	R	No	All selected patients	- Chest infection 22% - Falls 13% - Control of PD symptoms 10% - General medical problems 9% - Urinary dysfunction 8%
Kessler 1972 ²²	- PD - Paralysis agitans - Parkinsonism		468 patients	R	Yes	All selected patients	- PD 19% - Circulatory system 16% - Digestive system 10% - Accidents 9% - Respiratory system 8% - Remark: Neoplasm 4%: significant less than control group

Abbreviations: PD: Parkinson's disease, UTI: urinary tract infection, GI: gastrointestinal, R: retrospective, P: prospective.

^a Comparison with inclusion group concerning admission reasons.

Problems during hospitalization

We found one prospective study on acute events occurring during hospitalization.⁴ When admitted to a neurology ward (83 PD patients, mean age 69 years, mean disease duration 6 years), patients received an average of 0.6 non-neurological consultations. Reasons were: (aspiration) pneumonia, urinary infections and retention, diarrhoea, atrial fibrillation, postural hypotension, low back pain, and TIA. Specialists consulted most frequently

were cardiologists, internal medicine specialists and orthopaedic surgeons. Acute events observed during hospitalization on non-neurological department of 20 patients (mean age 80 years) after ER visits were: Urinary infection (33%), agitation, confusion and hyperthermia (28%), pressure ulcers and leg oedema (22%), bowel occlusion and hypotension (11%), and dysphagia (6%). Mortality rate during hospitalization of this last group was 20%. We found one retrospective study on this subject (173 PD patients), but this study is unclear on the presence or absence of complications before the hospital admission.²¹ Problems identified in this study do accord however with those described above.⁴

Another retrospective study shows that in 74% of 35 emergency hospital admissions of PD patients, their medication was stopped, omitted or prescribed inappropriately with 61% of this group suffering significant sequelae. Non-adherence to medication schedules was a large problem and in 11% of cases anti-dopaminergic medication (metoclopramide) was prescribed.³¹

In a study analyzing inpatient falls the use of anti-Parkinson's medication was an evident risk factor (OR 5.04).³²

Apart from the studies above we found several opinionated views and reviews on problems during hospitalization of PD patients. These authors point to disease fluctuations, stress⁷, and medications like butyrophenones, phenothiazines, and metoclopramide, prescribed during hospitalization, as possible causes of PD exacerbation.^{6,33-38} Additionally, sleep disorders, verbal communication problems, nutritional intake difficulties, and cognitive changes are mentioned as problem areas.^{7,19,39}

Perioperative problems

We found 15 retrospective studies on problems during and after surgery in patients with PD, with an emphasis on the postoperative period. Of these 15, 2 retrospective studies included a control group of non-PD patients.^{25,27} One retrospective study focused on postoperative confusion³³ and 2 retrospective studies on medication errors.^{40,41} Another study with 10 patients is actually a case report with 10 PD patients,⁴² and the remaining 9 papers are retrospective studies on PD patients undergoing orthopaedic surgery.^{29,43-50}

The first study compared 234 PD patients to a control group of 40,979, undergoing elective bowel resection, cholecystectomy, or radical prostatectomy, during a 6-year period. PD patients had a significantly increased incidence of aspiration pneumonia, urinary-tract infection, bacterial infections, with odds ratios of 3.8, 2.0, 1.7, respectively. Odds ratios for postoperative delirium and hypotension in PD patients were 2.6 and 2.5, with lesser significance. PD patients had a mortality rate of 7.3%, compared with a 3.8% in the control group.²⁵

In the second study with a non-PD control group, 51 PD patients, treated on different surgical departments, were compared using matched-pair analysis. There were significantly more postoperative falls in the PD group (18% vs. 4%), and a higher although not significantly increased number of urinary tract infections (33% vs. 24%), pneumonia (10% vs. 4%),

and also wound infection, urinary retention, respiratory insufficiency, and postoperative confusion. PD patients were hospitalized for more days and stayed on the intensive care unit longer.²⁷

Another retrospective study showed that 60% of 25 PD patients with no pre-existent mental status abnormalities suffered postoperative confusion, some with hallucinations. The onset of the delirium was often delayed, 70% after 36 hours. In this study, there was no relationship between delirium and type of anti-Parkinson medication or anaesthetic procedure.³³

In a retrospective study on pharmacological management during 51 surgical admissions of PD patients or patients with parkinsonian syndromes treated with PD medication, 71% had missed doses of their medication. Overall, antidopaminergic medication was prescribed in 41% and administered in 22% although not allowed. 47% (69% for non-day-cases admissions) had complications: neuropsychiatric 41%, falls 8%, and worsening of motor symptoms 5%.⁴⁰ A second study on pharmacological management found that 30% of 92 PD patients had medication administration problems, leading to an increase in postoperative confusion or worsening of PD: 84% to 36% in the well-managed group. Overall 31% of patients was dissatisfied in the way their PD was managed in the perioperative period.⁴¹

In the smallest study (n=10), all patients had complications. This paper identified the same problems as mentioned above, and additionally found pressure sores as an important problem.⁴²

Next to the above studies, there are 9 retrospective research articles on orthopaedic surgery and its complications. These studies (totalling 433 PD patients, Table 4) found pneumonia, urinary tract infections, confusion, and decubitus as the most frequent postoperative complications, in frequencies up to 49%⁴⁴⁻⁵⁰ with an overall 6 month mortality up to 47%.^{44,45,47,48,50,51} Apart from complications, several studies are contradictory regarding the outcome of orthopaedic procedures in PD patients,^{26,29,30,43-60} and postoperative rehabilitation is reported to be slower.^{28,55}

Next to these more or less formal surveys, case report and reviews mention the following perioperative problems: neuroleptic malignant syndrome, medication- or anaesthetic-induced exacerbation of PD, side-effects of PD medication, postextubation laryngeal spasm, bronchospasm, respiratory arrest, difficulty with salivation, gastrointestinal complications, deep vein thrombosis, urinary disturbances, temperature regulation problems, and tremor hampering eye surgery.^{6,8,34-38,61-80}

Improvement of care for the hospitalized PD patient

Improvement during hospitalization

There are no studies analyzing the effects of suggested recommendations/ improvements. Some authors favour a multidisciplinary approach during hospitalization.^{4,7} Other suggestions are: continuing the exact personal medication regime, education of nurses and doctors, being attentive for early signs of complications like pneumonia to start early treatment,

Table 4. Orthopedic surgery, complications

Study	Inclusion	Exclusion	Number	Design	Intervention	Most frequent complications
Mehta 2008 ⁴⁹	PD	Total knee arthroplasty revision	- 34 patients - 39 knees	R	Total knee arthroplasty	- Confusion 35% - Superficial wound infection, aspiration pneumonia both 6%
Weber 2002 ⁴⁸	PD	-	- 98 patients - 107 hips	R	Hip replacement	- 6 Month mortality 6% Overall complications: 36% - UTI 7% - Dislocation 6% - Postoperative confusion 4% - Pneumonia, deep venous thrombosis both 3%
Duffy 1996 ⁴³	PD	-	- 24 patients - 33 knees	R	Total knee arthroplasty	- Confusion 20% - Deep venous thrombosis, superficial infections both 8% - Myositis ossification, urinary retention, wound necrosis, respiratory tract infection all 4%
Turcotte 1990 ⁵⁰	PD	-	- 87 patients - 94 hips	R	Hip fracture surgery	After 6 months: - Mortality 14%: myocardial infarction (n=5), infection (n=2), pulmonary embolism (n=1), unknown (n=4) - Orthopaedic problem 14% - Decubitus ulcers 5% - Wound infections 4%
Vince 1989 ⁴⁶	PD	-	- 9 patients - 13 knees	R	Total knee arthroplasty	Deep vein thrombus (n=4), UTIs (n=3), temporary disorientation (n=2), skin necrosis (n=1), intestinal ileus (n=1), pulmonary embolism (n=2)
Staehele 1988 ⁴⁵	PD	Parkinsonism	- 49 patients - 50 hips	R	Hip fracture surgery	6 Months complication: - Mortality 20%: pneumonia 40%, congestive heart failure 20%, cerebrovascular accident 20%, pulmonary embolism 10%, cerebrovascular accident 10%, breast cancer 10% - UTI 20%, pneumonia 10%, decubitus ulcers 10%, pulmonary embolism 6%, cerebrovascular accident 6%, wound infection 4%
Eventov 1983 ⁴⁴	- PD - Ambulatory	Impacted subcapital fractures-	- 62 patients: 45 patients undergoing surgery	R	Hip fracture surgery	-3 Month mortality surgery group 31% (1 year 38%): bronchopneumonia 43%, congestive heart failure 21% - 3 Month mortality in patients not undergoing surgery 29% (35% 1 year)

						- Survivors surgery group (n=31): UTI 23%, decubitus 23%, bronchopneumonia 16%, contractures 6%, deep infection, cardiac arrhythmias, myocardial infarction, dislocation, thrombophlebitis, paralytic ileus all 3% - Survivors of patients not undergoing surgery (n=12): UTI 17%, decubitus 25%, bronchopneumonia 0%, contractures 17%
Coughlin 1980 ⁴⁷	- PD - Ambulatory	-	- 47 patients - 49 hips	R	Hip fracture surgery	- 6 Month mortality 47% - Decubitus 49% - Dislocation 37% (endoprosthesis)
Rothermel 1972 ⁴⁹	PD	-	- 23 patients: 16 without levodopa, 7 with levodopa	R	Hip fracture surgery	- With levodopa: phlebitis n=1 - Without levodopa: debrided decubitus ulcers n=2, phlebitis n=2, deep hematoma n=2, dislocation n=2, urinary septicaemia n=1, fatal myocardial infarction n=1

Abbreviation: PD: Parkinson's disease, UTI: urinary tract infection, R: retrospective.

falling prevention, (temporary) medication adjustment, emotional support, good sleep hygiene by maintaining the home bedtime and trying to prevent sleeping during the day, sometimes consulting a sleep disorder specialist or start sleeping medication, exercise, speech therapy, sufficient nutritional intake high in fibre, adequate fluid intake, preventing a confusional state by limiting the number of care-givers and the amount of light and noise during night sleeping, avoiding certain medication harmful for the PD patient, and consulting a neurologist.^{7,21,31,35,37,67}

Improvement of perioperative care

There are only 2 studies on medication continuation during surgery^{81,82} and one study analyzing the effect of an early postoperative neurologic consultation,²⁹ and numerous case reports, and opinionated views and reviews.

During preoperative screening, some authors recommend extra attention to be paid to this group of patients, especially to respiratory status, urologic system, fluid status, cardiovascular system, gastrointestinal system, autonomic system, and cognition.^{6,25,35,37,66,73,74,78,83} And, if necessary, supplemented with additional diagnostics like laboratory tests, pulmonary tests, electrocardiogram, and X-ray.^{25,66,73,78}

Most of the literature describes measures with regard to PD medication in the intraoperative period. To prevent large descents of dopamine levels intra- and postoperatively many

authors advise continuation of PD medication as long as possible preoperatively and resume it as soon as possible postoperatively, and PD medication is preferably continued.^{6,8,25,34,37,38,42,67-70,72-74,76,78,79,81,82,84-92} 2 studies on this topic describe PD patients using the rotigotine transdermal patch, a non-ergot D1/D2/D3 dopamine agonist.^{81,82} In the first prospective study, oral dopaminergic medication was easily switched to rotigotine before surgery and resumed afterwards in 14 PD patients undergoing surgery under general anaesthesia. Adverse events were 2 dopaminergic side effects namely nausea and hallucinations and one ventricular asystole.⁸¹ The second study on this topic describes PD patients derived from 2 prospective clinical trials. PD patients undergoing surgery under general anaesthesia and who continued using rotigotine during surgery were retrospectively analyzed (n=25). There was no worsening of PD symptoms, but (only) 3 complications: deep vein thrombosis, infection and pain.⁸²

As other substitutes for dopaminergic medication intraoperatively, continuous intravenous levodopa infusion, continuous subcutaneous infusion or immediate postoperative injections of apomorphine, and enteral levodopa/carbidopa via nasogastric tube or duodenostomy have been used by various authors,^{68,69,72,76,78,88,92,93} but none have been studied in a controlled trial. The use of parenteral anticholinergic and antihistaminic medication as anti-Parkinson therapy is limited according to some authors, and may aggravate postoperative discomfort because of autonomic side-effects and confusion.^{72,76,78}

Some authors claim that general anaesthesia should be avoided when possible, and prefer local anaesthesia.^{37,66,67,73,75,90} This is supported by a case report of a PD patient, undergoing surgery with regional anaesthesia, who was successfully given levodopa and carbidopa orally during the operation.⁸⁶ Regional anaesthesia also avoids postoperative nausea and vomiting.⁷³ Less invasive interventions, like laparoscopic surgery over abdominal surgery, are recommended.⁶⁶ Some authors advocate carefully considering the used operation technique.^{47,50}

In a retrospective study the postoperative period was analyzed in PD patients undergoing total knee arthroplasty receiving a preoperative or immediate postoperative neurologic consultation (n=13) compared with patients receiving a delayed or no visit (n=21). Only in the first group there was a significant improvement in total Unified Parkinson's Disease Rating Scale with most improvement in activities of daily living but also an improvement of mood, mentation and behaviour, and motor examination. In this group there was also a shorter length of stay (P<0.01) and less patients were confused: 15% to 48%.²⁹

There are many more recommendations, without formal studies. Postoperatively lung expansion manoeuvres, noninvasive mechanical ventilation, percussion, adequate pain control, aspiration precautions, (early) mobilization, recognition of unique physical limitations and medication combinations, physiotherapy, turning regimens, maintenance of volume status, antiparkinsonian therapy adjustments, analyzing urine for urinary tract infections, and deep venous thrombosis prophylaxis may prevent complications like pulmonary emboli, infections, deep vein thrombosis and decubitus.^{6,27,42-45,50,55,59,60,66,72,74,78,83,91,94-96} In

case of prolonged endotracheal intubation early tracheostomy is preferred.⁶⁶ Except for 2 case reports there is no literature concerning the pre-emptive administration of drugs to prevent complications. In one case report the cholinesterase inhibitor rivastigmine was given preoperatively to prevent delirium postoperatively in a PD patient successfully treated with this drug in two previous delirious episodes.⁹⁷ In another case report prokinetics were administered in 2 patients to prevent paralytic ileus.⁹² Some authors suggest preventive antibiotics to prevent infections.^{44,45,59} As described before, the onset of the postoperative delirium is often delayed. If patients are discharged rapidly after surgery, there should be sufficient support in the home environment.³³ Overall, team work between different specializations, like surgery, neurology, geriatrics, and a rehabilitation unit is generally advocated.^{28,96,98}

DISCUSSION

There are few studies analyzing the problems a PD patient encounters during hospitalization, and there are even less studies analyzing possible solutions. Most studies are retrospective and have small numbers of patients. In some studies PD patients were diagnosed according to clear diagnostic criteria (like the United Kingdom Parkinson's Disease Society Brain Bank's clinical diagnostic criteria),^{4,9-11,15,19,48} but in most studies the diagnostic criteria were not clearly mentioned: a neurologist confirmed the diagnosis,^{13,43,45,46,48} or medical record systems and/or patients notes were used to identify PD patients,^{17,20-22,25,27,33,40} or no information according to the diagnostic criteria, except the use of PD medication, was given.^{16,31,41,42,47,49,50,81,82}

Overall PD patients are more frequently^{20,23,24} and longer^{12,16,17,19,21,24-29} hospitalized compared with controls. Generally the leading causes for admission are injuries (many with fractures), infections (mainly pneumonia and urinary tract infections (UTI)), poor control of PD and complications of PD treatment, psychiatric disturbances, and diseases of the circulatory and digestive system. A reduction of the number of admissions might be achieved by extra attention to fall prevention, adequate drug regulation with acuity for side effects, preventing and recognizing of early symptoms of infections and active monitoring in the home situation of both patients' vital parameters and therapy compliance.^{5,18,20} When admitted to a hospital, most PD patients stay on a general medicine or surgery ward instead of a neurological one.^{5,15} Apart from one small prospective study⁴ and a retrospective study,³¹ little is known about problems occurring during hospitalization of PD patients not undergoing surgery, mentioning the usual direct and indirect PD related problems and medication issues.

There are more studies on complications in PD patients hospitalized for surgery, particularly in the postoperative period. (Aspiration) pneumonia, UTI, bacterial infections, postoperative falls, postoperative delirium/confusion (often with a delayed onset³³), and hypotension occur more frequently in this group of patients than in controls.^{25,27} Pressure sores are also

an important complication.⁴² Mortality rates are also higher.²⁵ These data are confirmed by studies on PD patients undergoing orthopaedic surgery.^{29,43-50} Many PD patients had post-operative medication administration problems with more postoperative confusion or worsening of PD as a result.^{40, 41} It is striking that almost one third of the PD patients were dissatisfied concerning their PD treatment.⁴¹

Suggestions for improvement of hospital care

There are many proposals for improvement during hospitalization in PD patients with or without surgery. Suggestions on improvement do vary, but most authors agree that attention should be given to all aspects of PD and not only to motor function.

Most publications refer to the intraoperative period mainly to prevent a decline in dopamine levels because of discontinuation of dopaminergic medication, including two studies favouring the use of a rotigotine patch.^{81,82} Most authors agree that anaesthesiologists and surgeons should take the increased vulnerability of PD patients into account when planning and selecting procedures.^{37,47,50,66,67,73,75,86,90} One small study shows that early consultation by a neurologist may prevent complications and reduce length of hospital stay.²⁹

CONCLUSIONS

Most studies were retrospective and had small numbers. Prospective studies with large numbers of PD patients, defined according to clear diagnostic criteria and preferably diagnosed by a specialist with special interest in PD, would be preferred for future research. Generally patients with PD are hospitalized much more frequently and longer than control groups. The leading causes are injuries, infections, poor control of PD and complications of PD treatment. The inclusion of hospitalization data into patient registries for PD could be a major improvement in identifying the important problems.

There are many (un-researched) proposals for improvement during hospitalization in PD patients. A substantial number of PD patients' admissions might be prevented. There should be guidelines concerning the hospitalized PD patients, with accent on early neurological consultation or consultation of another specialist like a geriatrician with a special interest in PD and team work between different specialities, and on sufficient training of all people involved in the treatment and recovery of this patient group. This protocol should include dopaminergic replacement therapy in case PD patients are not allowed or able to take their oral medication. Preferably this therapy should not be laborious and not invasive so that it is easily applicable.

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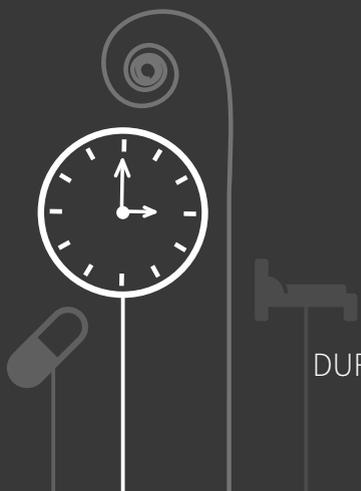
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CHAPTER 3

DETERIORATION OF PARKINSON'S DISEASE
DURING HOSPITALIZATION: SURVEY OF 684 PATIENTS

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ABSTRACT

Introduction

A substantial fraction of Parkinson's disease patients deteriorate during hospitalization, but the precise proportion and the reasons why have not been studied systematically and the focus has been on surgical wards and on Accident & Emergency departments. We assessed the prevalence and risk factors of deterioration of Parkinson's disease symptoms during hospitalization, including all wards.

Methods

We invited Parkinson's disease patients from 3 neurology departments in The Netherlands to answer a standardised questionnaire on general, disease and hospital related issues. Patients who had been hospitalized in the previous year were included and analyzed. Possible risk factors for Parkinson's disease deterioration were identified. Proportions were analyzed using the Chi-Square test and a logistic regression analysis was performed.

Results

18% of 684 Parkinson's disease patients had been hospitalized at least once in the last year. 21% experienced deterioration of motor symptoms, 33% did have one or more complications and 26% had received incorrect anti-Parkinson's medication. There were no statistically significant differences for these variables between admissions on neurologic or non-neurologic wards and between having surgery or not. Incorrect medication during hospitalization was significantly associated with higher risk (OR 5.8, CI 2.5-13.7) of deterioration, as were having infections (OR 6.7 CI 1.8-24.7). A higher levodopa equivalent dose per day was a significant risk factor for deterioration. When adjusting for different variables, wrong medication distribution was the most important risk factor for deterioration.

Conclusions

Incorrect medication and infections are the important risk factors for deterioration of Parkinson's disease patients both for admissions with and without surgery and both for admissions on neurologic and non-neurologic wards. Measures should be taken to improve care and incorporated in guidelines.

INTRODUCTION

Parkinson's disease (PD) patients are admitted to hospitals more frequently and longer than the general population.^{1,2} Up to a quarter of the total PD patients are hospitalized each year.¹ There is general consensus that a substantial fraction of these hospitalized PD patients do deteriorate, but the precise proportion and the reasons why have not been studied systematically and the focus has been on surgical wards and on Accident & Emergency departments.³⁻⁶ We found that, although many PD patients seem to deteriorate during hospitalization and there is concern about the quality of care provided to these patients⁷, most hospitals do not have proper guidelines yet to prevent worsening of PD symptoms and complications during hospitalization.⁸ Before such guidelines can be formulated, a better understanding of the problems encountered during hospitalization of this group of patients is warranted. Our aim in this study was to assess the prevalence and risk factors of deterioration in hospitalized PD patients including all wards.

METHODS

PD patients from 3 neurology departments in the southern part of The Netherlands were invited to participate in the survey, i.e. the Maastricht University Medical Centre in Maastricht, Orbis Medical Centre in Sittard-Geleen, and Catharina Hospital Eindhoven in Eindhoven. Only PD patients, of whom the diagnosis had been confirmed by a neurologist according to the UK Brain Bank criteria were selected. All patients with other or unclear parkinsonisms were excluded. The selected patients were sent a questionnaire by mail. This questionnaire consisted of questions concerning general, personal and disease related issues (see additional file 1 and 2). Patients were asked whether or not having cognitive problems. To obtain more accurate data, we asked patients to fill in the questionnaire with the help of a caregiver. Patients who confirmed that they had been admitted to a hospital in the previous year, were asked to answer more detailed questions about this hospital stay (e.g. exact timing or lack of drug administration, complications, and PD deterioration). After 4 weeks we sent a reminder to patients who had not yet returned the questionnaire. We validated the data by comparing the questionnaire-replies with corresponding hospital records. Only patients with a hospital submission in the previous year were included and analyzed. Admissions for PD related brain surgery were excluded. Subsequently, we tried to identify possible risk factors for PD deterioration.

PD deterioration we defined as decline in motor function. Receiving incorrect PD medication during the hospital stay was defined as administration of PD drugs during the hospital stay not as home schedule with attention to interruption, wrong timing, and different PD

medication. Levodopa Equivalent Dose (LED) was used to calculate the amount of anti-parkinsonian drugs.⁹

The ethics committees of the 3 collaborating hospitals approved our study: Medical Ethics Committee academic hospital Maastricht/Maastricht university (reference number 08-5-082), Local Advisory Group Scientific Research Orbis Medical Centre (reference number 10.029), and Medical Ethics Committee Catharina Hospital Eindhoven (reference number M11-015). Research was carried out in compliance with the Helsinki Declaration.

Statistical methods

We compared proportions using the Chi-Square test for independence and subsequently performed a logistic regression analysis. A *P*-value of less than 0.05 is considered statistically significant. Admissions were not included if there were data missing required for that specific analysis. All statistical analysis are performed with PASW-version 18.0 (SPSS, Chicago).

RESULTS

Response rate

We invited 884 patients to participate, and data from 684 patients (response rate 77%) were available for this study (Table 1). In total 123 patients were admitted to hospital in the previous year, accounting for 159 admissions, and these were used for analysis. 60% of the PD patients filled in the questionnaire together with a caregiver.

Hospitalization

18% of the PD patients were hospitalized at least once in the last year with an average of 1.3 (ranging between 1 and 4) admissions per patient per year. Patients were admitted most frequently on a non-neurological ward, being surgery (24%), internal medicine (22%), orthopaedics (15%), urology (13%), cardiology (11%) and others. Admission reasons for these wards were traumatic injury whether or not following surgery (20%), urinary tract problems (15%), gastrointestinal problems (15%), cardiac problems (12%), other surgical procedures (11%), elective joint replacement due to arthrosis (7%), pneumonia (6%), and others. 18% of the patients were admitted to a neurological ward. Of those, 71% had PD related problems (45% PD medication problems, 20% deterioration of PD, 10% PD related screening, 5% hallucinations/confusion, 5% swallowing problems, 15% unknown). Other reasons for admission to a neurological ward were mainly strokes.

More than a fifth of all patients experienced deterioration of motor PD symptoms during their hospital stay. 44% of them showed no complete recovery after discharge. Most patients stated to have an overall worsening of motor function (38%) or motor skills (32%).

The other ones had a worsening of rigidity (12%), tremor (9%), balance problems (3%), or bradykinesia (3%).

For the group of patients that were admitted because of PD deterioration, one patient further deteriorated during this admission. This patient didn't receive correct PD medication. A third of the patients did have one or more complications during the admission, mainly confusion followed by infections. Complications didn't differ between non-neurologic and neurologic wards ($P=0.83$). There was not more confusion ($P=0.80$) or other statistically significant differences in complication rates among patients whether or not having surgery. Of the patients having an infection as a complication during admission, none of them had an infection as admission reason.

More than a quarter of the patients reported receiving incorrect PD medication during the hospital stay, i.e. wrong timing (79%), different PD medication (29%) or interruption of PD medication (5%). No difference in medication distribution problems between neurologic and non-neurologic wards ($P=0.49$) or whether or not patients having surgery ($P=0.07$) was found. In 3% there was self-administration of PD drugs.

Deterioration and relating factors

With respect to the general and PD related characteristics only for patients with a LED-value of more than 700mg/day there is a significantly increased risk for deterioration of PD symptoms (Table 2).

As to hospital related risk factors incorrect medication administration during hospitalization was significantly associated with deterioration during admission. This was also the case when one or more complications occurred. Analyzing the individual complications, only infections showed to be a significantly increased risk factor. No other variables were significant.

In 14% of the admissions, PD patients had both cognitive problems and didn't have the help of a caregiver to fill in the questionnaire. When excluding this group of patients, since the reported data maybe less reliable, both medication problems during admission ($P=0.00$, odds-ratio 6.0, 95%-confidence interval 2.4-14.9) and a LED-value of more than 600mg/dag ($P=0.024$, odds-ratio 3.25, 95%-confidence interval 1.2-9.0) are significant risk factors for deterioration, and infections aren't ($P=0.08$).

When adjusting for possible confounders (logistic regression was applied using the following variables: Age, gender, PD duration, LED-value, Hoehn& Yahr scale, presence of cognitive problems, recruitment centre, wrong medication distribution, complications, infections, surgery, non-neurologic ward admission, consultation of PD nurse specialist and involvement of paramedics), there was still a significantly increased risk of deterioration in PD patients who had received incorrect medication ($P=0.042$).

Validation

We were able to retrieve clinical files of 84 (52%) admissions. Most of the other files got lost because of an intermittent change in computerized medical systems. In those files, which

Table 1. Patient and hospitalization characteristics

	MUMC		OMC		CHE		Total	Homogeneity ^c	
Total questionnaires (n)	447		230		207		884		
Response rate (%)	72		84		81		77		
Admitted patients (n)	53		34		36		123		
Total hospitalizations (n)	61		47		51		159		
Age (yr)	71 [SD=10.4]		75 [SD=7.6]		71 [SD=8.5]		72 [SD=9.2]		0.87
Disease duration (yr)	9.6 [SD=7.0]		9.1 [SD=7.2]		10.7 [SD=6.9]		9.8 [SD=7.0]		0.49
LED-value (mg/day)	554		761		855		711		0.004
	n ^a	% ^a							
Gender									
Women	28	46	15	32	14	28	57	36	0.04
Men	33	54	32	68	37	72	102	64	
Hoehn&Yahr									
stage < III	24	39	20	43	13	25	57	36	0.12
stage III, IV	33	54	25	53	33	65	91	57	0.32
stage V	3	5	2	4	5	10	10	6	0.33
Don't know / missing	1	2	0	0	0	0	1	1	
On-off fluctuations									
Yes	27	44	14	30	21	41	62	39	0.61
No	33	54	33	70	30	59	96	60	
Don't know / missing	1	2	0	0	0	0	1	1	
Cognitive problems									
Yes	20	33	24	51	29	57	72	46	0.009
No	41	67	23	49	22	43	86	54	
Don't know / missing	0	0	0	0	0	0	0	0	
Deterioration during admission									
Yes	13	21	10	21	11	22	34	21	0.84
No	45	74	30	64	35	69	110	69	
Don't know / missing	3	5	7	15	5	10	15	9	
Complications during admission									
None	40	66	30	64	35	69	105	66	0.76
One or more complications	21	34	15	32	16	31	52	33	0.30
Confusion	13	21	11	23	11	22	35	22	0.91
Urinary tract infection	4	7	6	13	2	4	12	8	0.70
Emotional disturbance	6	10	0	0	0	0	6	4	0.004
Pneumonia	0	0	2	4	2	4	4	3	0.17
Memory complaints	2	3	0	0	3	6	5	3	0.50
Falls	0	0	2	4	0	0	2	1	0.87
Other	2	3	0	0	3	6	5	3	0.50
Don't know / missing	0	0	2	4	0	0	2	1	
Medication distribution									
Good	40	66	29	62	39	76	108	68	0.15
Bad	18	30	16	34	8	16	42	26	
Don't know / missing	3	5	2	4	4	8	9	6	
Surgery									

Yes	39	64	21	45	31	61	91	57	0.63
No	22	36	26	55	20	39	68	43	
Don't know / missing	0	0	0	0	0	0	0	0	
Ward									
Neurologic	11	18	6	13	11	22	28	18	0.68
Non-neurologic	48	79	41	87	39	76	128	81	
Don't know / missing	2	3	0	0	1	2	3	2	
Involvement of paramedics									
Yes	23	38	29	62	8	16	60	38	0.025
No	34	56	14	30	41	80	89	56	
Don't know / missing	4	7	4	9	2	4	10	6	
Consultation of PD nurse specialist^b									
Yes	14	23	20	43	5	10	39	25	0.14
No	45	74	24	51	44	86	113	71	
Don't know / missing	2	3	3	6	2	4	7	4	

^a N; number and percentage of total admissions

^b Non-neurological ward

^c For homogeneity between different centres the Pearson Correlation and Spearman's rho tests were used. P-values are shown. P-value <0.05 is considered significant.

Abbreviations: MUMC: Maastricht University Medical Centre, OMC: Orbis Medical Centre, CHE: Catharina Hospital Eindhoven, n: number, SD: standard deviation, LED-value: Levodopa Equivalent Dose, PD: Parkinson's disease.

thus comprise a sample half the size of our patient sample, a doctor only once documented deterioration of PD. There was no report of deterioration by a nurse (vs. 34 by the patients). PD medication distribution problems were mentioned 7 times by a doctor and 12 times by a nurse (vs. 42 by the patients). Urinary tract infections were reported 8 times (vs. 12), confusion 13 times (vs. 35), pneumonia 3 times (vs. 4) and furthermore 3 others.

Table 2. Effect of patient, Parkinson’s disease characteristics, and factors during hospitalization on deterioration of Parkinson’s disease

Possible risk factors	Deterioration (n=34)		
	N	P-value ^a	OR [95%-CI]
Gender			
Male	25	0.39	
Age			
≥70 years	20	0.42	
≥80 years	5	0.47	
≥85 years	5	0.13	
Disease duration			
≥8 years	17	0.82	
≥10 years	9	0.18	
≥12 years	8	0.36	
Hoehn&Yahr			
stage ≥II	27	0.50	
stage ≥III	27	0.07	
On-off fluctuations	16	0.38	
Cognitive problems	19	0.18	
LED-value			
>500mg/day	15	0.60	
>600mg/day	15	0.07	
>700mg/day	15	0.003	4.4 [1.7-11.5]
Complications ≥ 1	16	0.04	2.5 [1.1-5.6]
Confusion	10	0.23	
Infections	7	0.00	6.7 [1.8-24.7]
Wrong medication distribution	18	0.00	5.8 [2.5-13.7]
Surgery	17	0.26	
Non-neurologic ward	27	0.60	
No involvement of paramedics	16	0.15	
No consultation of PD nurse specialist^b	17	0.04	0.3 [0.1-0.7]

^a P-value <0.05 is considered significant

^b Non-neurological ward

Abbreviations: N: number, OR: Odds-ratio, 95%-CI: 95%-confidence interval, LED: Levodopa equivalent dose, PD: Parkinson’s disease.

DISCUSSION

We sought to assess the prevalence and risk factors of deterioration in hospitalized PD patients, as evidence suggests that a substantial proportion of PD patients actually worsen when admitted to a hospital.^{1,2} In our population of 684 PD patients almost one fifth had been hospitalized in the last year. Traumatic injury, infections, direct PD-related problems, and problems with the circulatory and digestive system were the main admission reasons, which accords with prior literature.^{1,2} As in those studies, confusion and infections were the most common complications during hospitalization.¹

To our knowledge this is the first study systematically analyzing different risk factors for deterioration of PD patients both for admissions with and without surgery.

There have been earlier studies documenting high rates of incorrect medications given to hospitalized PD patients, some as high as 74%. All these, on surgical wards and on Accident & Emergency departments, found that this was associated with deterioration, but to varying degrees. All these studies were retrospective, and selection of the patient sample was unclear.³⁻⁵ We found having surgery or not did no matter in terms of medication distribution problems or complications. Somewhat unexpected, neurology wards do not do better, as there was no statistically significant difference between different wards regarding problems with medication distribution, complications, and PD deterioration.

There is one retrospective study suggesting that pre-operative or immediate post-operative neurological consultation of PD patients having surgery may result in higher post-operative improvement of total Unified Parkinson's Disease Rating Scale with most effect on activities on daily living.⁶ In our study PD nurse specialists (as part of the movement disorder teams) were involved in a quarter of the admissions on a non-neurological ward. This was associated with a higher risk on deterioration during these admissions. This is probably reverse causation, since PD nurse specialists were asked to see the patient when deterioration had already occurred.

Second to medication distribution problems with a 5.8 higher risk on deterioration, complications are significantly related to PD deterioration, with infections as mean factor with an increased risk of 6.7. Paramedic care did not appear to be of influence. When analyzing different patient and PD related factors in relation to deterioration, only a LED-value above >700mg/day showed to be a significant risk factor. For higher age and higher Hoehn and Yahr scores there was a tendency towards, but not a significantly, higher risk. When excluding those patients who had no help with answering the questionnaire and had cognitive problems, only wrong medication distribution and a LED-value of more than 600mg/dag are significant risk factors.

There are significant differences for some variables between the hospitals which can be expected since the Maastricht University Medical Centre is, unlike the others, an university hospital (with more complex PD patients and more patients with deep brain stimulation).

There is however no significant difference between the centres in medication distribution problems.

When correcting for different variables, including those that were significant different between the three centres, wrong medication distribution is the most important significantly increased risk factor for deterioration. Comparing our data with data on medication errors in hospitalized patients in general, showing medication errors on average in 6 per 100 hospitalized patients, this study supports the higher vulnerability of PD patients.¹⁰

When validating the reported data by PD patients with clinical files of the admissions there seems to be mainly a strong underreporting of deterioration of PD supporting the lack of knowledge of this problem.

Apparently much more needs to be done to prevent incorrect medication distribution and complications. Better education of health care professionals, both on a neurological and non-neurological wards, to stress the importance of correctly administrated PD drugs and to prevent complications might result in less deterioration. Rigid electronic medication systems in hospitals do not seem to support home schedules of PD medication. Self-administration of PD drugs by able patients could be an option. The effects of an electronic warning system to alert the treating team of the vulnerability of this patient group, and a multidisciplinary approach, with a role for the clinical pharmacist and movement disorder team, should be evaluated in future studies.

This study has a number of limitations. Information was asked about the previous year, causing possible recall bias. Medication administration was assessed through self-report, and patients who died during admission were obviously not included. Since it was not possible to uncover adverse medication prescription during the admissions this aspect was not taken into account. Further studies should be undertaken to shed more light on these aspects. Nevertheless, we believe that these limitations do not invalidate our conclusions.

CONCLUSIONS

This is the first study systematically analyzing different risk factors for deterioration of hospitalized PD patients both for admissions with and without surgery. There is a high rate of deterioration during hospitalization of PD patients on all wards. Especially incorrect medication distribution, but also infections are related to this. Measures should be taken to improve care and should be incorporated in guidelines.

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CHAPTER 4

MOTOR OUTCOMES DURING HOSPITALIZATION IN PARKINSON'S DISEASE PATIENTS: A PROSPECTIVE STUDY

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ABSTRACT

Introduction

Retrospective studies suggest that many Parkinson's disease patients have a worsening of their motor status during hospitalization. We aimed to quantify this prospectively, and study possible contributing factors.

Methods

Over one year we included all consecutive Parkinson's disease patients, newly admitted to a Dutch teaching hospital. We analyzed complications, interventions, and medication distribution. At inclusion and at discharge we assessed the motor status with the Unified Parkinson's Disease Rating Scale Part III (UPDRS-III).

Results

48% of 46 admitted patients had complications, mainly confusion/delirium (24%) and infections (15%). At discharge 28% of the patients had a worse motor function with a mean increase of more than 5 points on the UPDRS-III. Medication errors occurred in 39%. This is the most important risk factor ($p < 0.000$) for motor function deterioration, followed by infections during hospitalization, and not being in control of own Parkinson's disease medication. 24% of patients were allowed to take control of their own Parkinson's disease medication, none of these patients did deteriorate.

Conclusions

This prospective study shows that a substantial part of hospitalized PD patients has a significant worse motor function at discharge mainly due to medication errors and infections. Quality of care could be improved by addressing preventable errors and allow patients to take control of their own Parkinson's disease medication.

INTRODUCTION

Parkinson's disease (PD) patients are hospitalized more frequently, have longer admissions, and suffer more complications during hospitalization compared to control groups.¹ Retrospective studies suggest that a substantial part of admitted PD patients also have a worsening of their motor status during these admissions, and that this is mainly due to medication distribution errors and infections.²⁻⁵

These studies were all retrospective and motor status was assessed through self-report or from medical records. To our knowledge no data are available on the severity of motor function deterioration during hospitalizations. Therefore, the aim of this study was to analyze prospectively whether or not there is deterioration of motor function at discharge of hospitalized PD patients compared to admission, and if so, to assess its severity and related factors.

METHODS

Participants

Over a period of one year, we invited all consecutive patients with PD, admitted to the Maastricht University Medical Centre in Maastricht, The Netherlands, to participate. Only admissions related to deep brain stimulation and daycare admissions were excluded.

Selection

Daily, except for some weekends, the hospital medication system was searched for newly registered anti-Parkinson medication and related new admissions of PD patient. For departments not using this system, all newly admitted patients were analyzed daily for having PD on the basis of medical history list, prior documentation and admission information. In addition, neurologists on the emergency department and on wards were asked to look out for admitted PD patients. When a possible participant was identified, this patient was examined for fulfilling the UK Brain Bank criteria for PD and if so, asked to participate: written informed consent was obtained.

Data collection

We collected patient data at two timepoints, i.e. day one of participation (moment 1) and the day before or day of discharge (moment 2). Each patient was interviewed and examined by the same doctor (OG or MB) at both occasions. At first visit we asked questions about general and disease related issues. At both timepoints we interviewed patients about admission related issues e.g. deterioration of PD, complications, and medication administration with the help of a questionnaire (see additional file 3) and hospital records.

If possible or necessary, this interview took place in the presence of a caregiver to provide any extra information. We assessed the patient's motor function through the Unified Parkinson's Disease Rating Scale Part III (UPDRS-III) at both timepoints. Hoehn and Yahr-scores were also taken. Almost daily, we reviewed the hospital records (both from doctors and nurses) of the included patients for complications, interventions, and (contra-indicated) medication prescription and distribution. Also almost daily, the same investigating physician who saw the patient at moments 1 and 2, checked the admitted patient without doing a formal physical examination. Therefore, information about possible adverse events and complications during admission between measurement moments 1 and 2 were retrieved from patients, caregivers, and hospital records and were combined. In case of a difference between patient information and hospital records, the visiting doctor (OG or MB) decided on the basis of his experience during the almost daily visits.

We defined PD deterioration as a clinically important decline in motor function: UPDRS-III score increase between moments 1 and 2 of at least 2.5 points, i.e. minimal clinically important difference. We also analyzed moderate clinically important difference, i.e. minimum of 5.2 points higher score on the UPDRS-III on moment 2.⁶ Improvement of motor function was defined as UPDRS-III score decrease between moments 1 and 2 of at least 2.5 points. We were not able to assess all UPDRS-III items in all patients at both timepoints, as sometimes the reasons for admittance interfered with this, e.g. fractures or surgery. To analyze the differences in motor score between inclusion and discharge per patient only those items were taken into account that could have been measured on both moments for this patient.

Receiving incorrect PD medication during the hospital stay was defined as any administration of PD drugs during hospital stay not identical to the original schedule before admission with attention to interruption, wrong timing, and different PD medication between moments 1 and 2. The hospital registration system for medication distribution was compared with patients' (or caregivers') information about their home medication schedule. So, if a patient at home sometimes missed a dose of PD medication or wasn't that strict with timing, this was not counted as an error during hospitalization. Subsequently, we tried to identify possible risk factors for PD deterioration.

Ethical approval

The Medical Ethics Committee of the Maastricht University Medical Centre (reference number 10-05-010) approved this study.

Statistical analysis

The Chi-Square test was used. A p-value of less than 0.05 is considered statistically significant. All statistical analysis are performed with PAW-version 18.0 (SPSS, Chicago).

RESULTS

Inclusion

From the first of December 2010 till the first of December 2011, 62 admissions met the selection criteria: 10 were not included since no informed consent was acquired from these patients or their family. Therefore, 52 admissions were included accounting for 40 PD patients. 31 patients were admitted once, the other ones 2 (n=6) or 3 times (n=3). For 6 admissions there was no measurement moment 2 since this was the same day or the day after measurement moment 1.

During 89% of these 46 admissions with a second measurement moment, patients were included within the first 24 hours of admission: Day 1 (i.e. the day of admission) 18 patients and day 2 23 patients. Because of some admissions during the weekend or Friday evening (and no researcher was available) a few patients were included later: day 3 (4 patients) or day 4 (1 patients).

For admission reasons see Table 1.

Admission related characteristics

For general, PD, and admission related characteristics see Table 2.

48% of the admitted patients had complications, mainly confusion/delirium (24%) and infections (15%), see also Table 1. At discharge more than a quarter of the patients had a worse motor function with a mean increase of more than 5 points on UPDRS-III. Of those, most frequent were worsening of hand movements (62%), rigidity (54%), rest tremor (54%), finger tapping (54%), pronation-supination hand movements (46%), and kinetic tremor (46%). There was an improvement of motor function in less than one quarter of the admissions.

PD medication errors occurred in 39% of the admissions, largely consisting of wrong timing and less frequently by omissions. PD medication errors, infections during hospitalization, and not being in control of own PD medication are the only significant risk factors for motor function deterioration (see table 3), with the highest association (phi coefficient) for PD medication errors: 0.77, 0.41 and 0.36 respectively.

When analyzing a moderate clinically important worsening of motor function, 15% deteriorated and medication errors were still a significant risk factor ($p=0.001$).

24% of patients were allowed to take control of their own PD medication, none of these patients did deteriorate. There were significant less medication errors, more emergency admissions, and more surgeries including surgeries under general anesthesia in this group. For all the other different variables in Table 3 there was no significant difference.

4 patients had more than one admission and during one admission a medication error and during another they did not. During admissions with medication errors all these patients

Table 1. Admission reasons and complications

Medical specialism	Number of admissions (%)	Admission reasons ^a	n	Complications	n
Orthopedics	11 (23.9)	Hip replacement	3	Confusion/Delirium	5
		Hip fracture surgery	2	Hallucinations	3
		Lumbar stenosis surgery	2	Decubitus	2
		Patella fracture surgery	2	Anemia	1
		Rotator cuff arthropathy surgery	1	Epididymitis	1
		Scoliosis surgery	1	UTI	1
			1	Wound infection	1
Surgery	6 (13.0)	Choledochus occlusion	3	Confusion/Delirium	3
		Anemia	1	Hallucinations	2
		Aortic aneurysm surgery	1	Anemia	1
		Rib fracture	1	Constipation	1
		Sarcoma surgery	1	Drain infection	1
					1
				Hypotension	1
				UTI	1
Cardiology	6 (13.0)	Cardiac asthma	3	Confusion/Delirium	1
		Angina pectoris	2	Decubitus	1
		Anemia	1	Hypoglycemia	1
		Heart failure	1	Phlebitis	1
				UTI	1
Internal medicine	5 (10.9)	Anemia	1	Hypotension	2
		Delirium	1	Confusion/Delirium	1
		Decubitus	1	Mood disorder	1
		Eye surgery	1		
		Erysipelas	1		
		Gastrointestinal bleeding	1		
		Hydronephrosis	1		
		Urosepsis	1		
Pulmonology	5 (10.9)	Pneumonia	3	Confusion/Delirium	1
		Malignant pleural effusion	1	UTI	1
		Pneumothorax	1		
Neurology	4 (8.7)	Worsening of PD	2	Decubitus	1
		Delirium/confusion	2	Hallucinations	1
		Cellulites	1		
		Hallucinations	1		
		Eye surgery	1		
		Orthostatic hypotension	1		
Gynecology	4 (8.7)	Vaginal blood loss	1	Air under skin	1
		Uterus extirpation	1	Diplopia	1
		Diagnostic laparoscopy	1	Splenic rupture	1
		Ovary cancer	1	Syncope	1
Urology	3 (6.5)	Urosepsis	2	Paresthesia hand	1
		Kidney stones	1		
Ophthalmology	2 (4.3)	Cataract surgery	2	-	
Total	46 (100)				43

Only admissions having a second measurement (moment 2) were included.

^aSome patients had more than one admission reason.

Abbreviations: N: number, PD: Parkinson's disease, UTI: urinary tract infection.

Table 2. General, PD, and admission related characteristics

Characteristics		n
Male: %	54.3	25
Mean age: Years (SD)	74.0 (6.3)	46
Disease duration ^a : Years (SD)	8.0 (7.5)	45
Hoehn and Yahr scale at admission: Stage (SD)	3.0 (1.1)	46
UPDRS-III score at admission: Score (SD) of total (SD)	31.6 (12.8) of 101.7 (11.2)	46
UPDRS-III score at discharge: Score (SD) of total (SD)	32.7 (12.7) of 103.5 (10.7)	46
Patients with on-off periods: %	13.0	6
LED-value ^f : mg/day (SD) at admission	545,8 (301,4)	46
PD medication:		
Levodopa: %	93.5	43
Dopamine agonist: %	43.5	20
Others: %	8.7	4
Not using PD medication: %	2.2	1
Higher LED-value at discharge: %	2.2	1
Lower LED-value at discharge: %	0	0
Number of patients with non per os during admission		0
Hospitalization: Days (SD, minimum, maximum)	8.7 (6.0, 2, 25)	46
Emergency admissions: %	63.0	29
Surgery: %	54.3	25
General anesthesia: % of surgeries	80.0	20
Local anesthesia: % of surgeries	20.0	5
Fall incidences: %	4.3	2
Motor function:		
Deterioration ^b : %, change in UPDRS-III (minimum, maximum)	28.3, 5.5 (3, 11)	13
No change ^c : %, change in UPDRS-III (minimum, maximum)	50.0, -0.3 (-2, 1)	23
Improvement ^d : %, change in UPDRS-III (minimum, maximum)	21.7, -6.0 (-3, -15)	10
PD medication error ^e : %	38.6	17
Wrong timing: % of medication error	70.6	12
Some rounds not distributed: % of medication error	58.8	10
Number of doses per day too low: % of medication error	11.8	2
Contraindicated medication ^f :		
Metoclopramide: n prescribed; n administrated		2, 0
Haloperidol: n prescribed; n administrated		1, 1
Control of own PD medication: %	23.9	11
Involvement of allied health services:		
Physical therapy: %	45.7	21
Occupational therapy: %	4.3	2
Speech therapy: %	2.2	1
Involvement of PD nurse specialist: %	2.2	1

Only admissions having a second measurement (moment 2) were included.

^a For one patient there is an unknown disease duration.

^b Mean individual UPDRS-III difference between moments 1 and 2: Worsening of at least 2.5 points.

^c Mean individual UPDRS-III difference between moments 1 and 2: Change between -2.5 and 2.5 points.

^d Mean individual UPDRS-III difference between moments 1 and 2: Improvement of at least 2.5 points.

^e One patient did not have PD medication and for one patient it was unclear if there was a medication error during admission.

^f No other dopamine antagonists, anti-emetics or atypical antipsychotics were prescribed.

Abbreviations: SD: standard deviation, LED: Levodopa Equivalent Dose, PD: Parkinson's disease, N: number.

deteriorated, during the others none did, with a mean individual UPDRS–III difference between moments 1 and 2 of 4.6 and -0.75 respectively ($p=0.01$). None of them had an infection.

One patient had his PD medication changed on purpose during admission: Levodopa was increased and anticholinergic drugs were stopped (not analyzed as medication error) because of problems at home. This patient's motor function improved. When excluding this patient and those who were not included within the first 24 hours after admission, PD medication errors, infections during hospitalization, and not being in control of own PD medication are still the only significant risk factors for motor function deterioration: $p=0.000$, $p=0.01$ and $p=0.02$ respectively.

Patients that improved during hospitalization, had significantly more emergency admissions and transfer to another department during hospitalization: Since a lot of patients with an emergency admissions to the Maastricht University Medical Centre are initially admitted to a temporary ward, these two factors are correlated. Of those, 40% had an infection as an admission reason: Proportionally more but not significantly higher compared to elective admissions ($p=0.06$). One patient his PD medication was adjusted and improved (as described before).

We found that PD patients experiencing a medication error were hospitalized longer than those without, respectively 9.6 and 7.9 days, but this difference was not significant ($p=0.40$). 7 PD patients admitted to non-neurology departments were seen by a neurologist or geriatrician. Once this was before motor deterioration occurred and once after, the other 5 visits were for other neurological reasons.

During 4 admissions the researchers notified the treatment team of a PD medication error since the PD patient had deteriorated. Furthermore, twice contraindicated medication was prescribed and therefore recommended not to give.

Table 3. Motor function of hospitalized PD patients and related factors

		Number of admissions ^a	Number of patients deteriorated	p-value ^b
Gender	Male	25	6	0.48
	Female	21	7	
Age ^c	<75 years	25	6	0.48
	≥75 years	21	7	
Disease duration ^{c,d}	<8 years	32	9	1.00
	≥8 years	13	4	
Patient with on-off periods	No	40	11	1.00
	Yes	6	2	
Hoehn & Yahr at admission ^c	Stage <4	30	8	0.74
	Stage ≥4	16	5	
LED-value at admission ^c	<700 mg/day	31	10	1.00
	≥700 mg/day	15	3	
Admission duration ^c	<10 days	32	7	0.17
	≥10 days	14	6	
Emergency admission	No	17	4	0.74
	Yes	29	9	
Neurology department	No	42	13	0.31
	Yes	4	0	
Surgery	No	21	8	0.18
	Yes	25	5	
General anesthesia	No	26	9	0.28
	Yes	20	4	
Complications	No	24	4	0.07
	Yes	22	9	
Infections during hospitalization	No	39	8	0.01
	Yes	7	5	
PD medication error ^e	No	27	0	0.000
	Yes	17	13	
Not in control of own PD medication ^f	No	11	0	0.02
	Yes	34	13	
Transfer to other department	No	37	10	0.70
	Yes	9	3	
Physical therapy during hospitalization	No	25	5	0.18
	Yes	21	8	
Overall		46	13	

^aOnly admissions having a second measurement (moment 2) were included.

^bP-value <0.05 is considered significant. The Chi-Square test was used.

^cBoth higher and lower cut of points were analyzed but p-values were not significant.

^dFor one patient there is an unknown disease duration.

^eFor one patient it was unclear if there was a medication error during admission and one patient didn't use PD medication.

^fOne patient did not have PD medication.

Abbreviations: LED: Levodopa equivalent dose;; SD: standard deviation, PD: Parkinson's disease.

DISCUSSION

This prospective study confirms prior reports about the high number of complications and medication errors during hospital admission of PD patients.^{1-4,8} Many patients had a worse motor function at discharge, which is not what one expects from a hospital stay. Medication error was the most important significantly related risk factor for deterioration, followed by infections during hospitalization, and not being in control of own PD medication. For patients who were allowed to take control of their own Parkinson's disease medication, there were significantly less medication errors and therefore these factors seem to be positively correlated. The role of medication errors was supported by analysis of patients with multiple admissions, who did not deteriorate when no medication error occurred.

Patients that improved during admission, all had emergency admissions because of acute disease related reasons and this may have caused worsening of PD symptoms prior to admission.

We included most, but not all patients within the first 24 hours of admission. Therefore, moment of inclusion was used as a start point for data collection during admission including possible adverse events and complications.

Since UPDRS-III observations were not blinded and could have biased the results when interpreting the data, we applied two different definitions of motor worsening: minimal and moderate clinically important difference. For both, PD medication errors during admission were a significant risk factor for motor deterioration. This accords with a prior retrospective study.³

A limitation of our study is its modest size and we could have missed some admissions. This relatively small study does confirm earlier retrospective studies, and we think that the prospective nature might even have biased the outcome in a positive way. The differences might have been bigger if no interventions would have taken place and the ward doctors wouldn't have noticed the researchers. We also think that these results from one hospital only are generalizable, as prior articles from other centres report similar problems^{2,4,8,10} and our earlier retrospective study showed no difference between this centre and two others.³ To improve quality of provided care during hospitalization early involvement of PD specialists seems important,^{9,10} with special attention for the original medication schedule of the patient. Infections should be prevented as much as possible and PD patients should perhaps be allowed to control their own medication.

CONCLUSION

This prospective study shows that a substantial part of hospitalized PD patients has a significant worse motor function at discharge mainly due to medication errors and infections.

Quality of care could be improved by addressing preventable errors and allow patients to take control of their own Parkinson's disease medication.

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CHAPTER 5

COGNITIVE FUNCTIONS IN PARKINSON'S DISEASE
PATIENTS DURING HOSPITALIZATION:
A PROSPECTIVE STUDY

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Submitted

ABSTRACT

Introduction

Motor function deterioration of PD patients during hospitalization is now well documented. There is anecdotal evidence that hospitalized PD patients also have cognitive deterioration. We aimed to prospectively assess the prevalence of cognitive decline in patients with Parkinson's disease during hospitalization.

Methods

During one year we included 42 PD patients admitted to the Maastricht University Medical Centre. Both at admittance and discharge we assessed cognitive functioning with Mini-Mental State Exam and the Scales for Outcomes of Parkinson's disease-Cognition. We also collected general and disease related information, did a neurological examination and recorded complications and medication errors.

Results

We found cognitive deterioration at discharge on both Mini-Mental State Exam (42 admissions) and Scales for Outcomes of Parkinson's disease-Cognition (31 admissions) in 21% and 29% of the cases respectively. At least half of the patients experienced complications. More than a quarter had delirium or an episode of confusion. This was a significant risk factor for overall cognitive decline during hospitalization. Parkinson's disease medication errors were associated with worse test results on Mini-Mental State Exam and delirium/episode of confusion. Patients with cognitive deterioration had an increased length of hospital stay.

Conclusions

A substantial part of the hospitalized PD patients have cognitive deterioration at discharge associated with delirium or episode of confusion resulting in a longer length of hospitalization.

INTRODUCTION

One of Parkinson's disease (PD) potentially most invalidating non-motor symptoms is cognitive impairment.^{1,2,3} Mild cognitive impairment is present in about one quarter of all PD patients, and dementia can be diagnosed in up to 83% of PD patients with longer disease duration.²⁻⁵

Recent research has now extensively documented the contra-intuitive observation of deterioration of PD patients as they are admitted to a hospital.⁶⁻⁸ They are hospitalized more frequently and generally for longer periods than those without PD.^{6,9} We found that up to one quarter of all hospitalized PD patients experienced a substantial deterioration in motor function, both through medication errors and infections.^{7,8} Cognitive decline is a generally acknowledged complication of hospital admittance of the elderly patient^{10,11}, but to our knowledge, this phenomenon has never been studied specifically in hospitalized PD patients. Since cognitive impairment in PD patients is associated with a reduced quality of life and increased caregiver burden¹², assessment of possible cognitive decline during hospitalization and analysis of possible risk factors is important.

The objective of this prospective study was to determine the prevalence of cognitive decline in PD patients during hospitalization and to identify possible risk factors.

METHODS

A detailed description of the methods used in this study has been published: See Chapter 4.⁸

Participants

During the one year study period from December 2010 till December 2011 PD patients who were admitted to the Maastricht University Medical Centre in Maastricht (MUMC), The Netherlands, and met the United Kingdom PD Brain Bank criteria were asked to participate. During the inclusion period we searched almost daily for newly admitted PD patients. To identify these PD patients different methods were used. The hospital medication system was analyzed to find those patients using anti-Parkinson medication. For some departments all medical records of newly admitted patients were screened for having PD. Next to this, the neurologist on the emergency department and the consulting neurologist were asked to report admitted PD patients. Excluded were those patients who were admitted for deep brain stimulation and/or daycare admissions. All included patients provided informed consent prior to taking part in this study.

Data collection

During the first contact (moment 1), as soon as possible after admission, we interviewed the patient and asked about general and disease related issues. Additionally we did a neurologic examination, and assessed the following clinimetric tests: the Unified Parkinson's Disease Rating Scale Part III (UPDRS-III), a Mini-Mental State Exam (MMSE), and the Scales for Outcomes of Parkinson's disease-Cognition (SCOPA-Cog). MMSE is frequently used to test changes of cognitive function during hospitalization.^{13,14} SCOPA-Cog on the other hand is more sensitive for cognitive deficits in patients with PD.¹⁵⁻¹⁸ We repeated this for each patient the day before or day of discharge (moment 2). During this last contact we also asked the patient about issues regarding the admission (e.g. complications, medication administration). If possible a caregiver was asked for extra information.

Almost daily we collected information from the hospital records with regard to interventions, complications, and medication prescription and distribution and one of us visited the patient to gain an overall impression of the patient.

PD medication administration during hospitalization between moment 1 and 2 was compared to the patient's home medication schedule and interpreted as inappropriate in case of a difference with regard to interruption, timing, and different PD medication.

Ethical approval

This study was approved by The Medical Ethics Committee of the Maastricht University Medical Centre (reference number 10-05-010), Maastricht, The Netherlands.

Statistical analysis

Statistical analysis was performed using the statistical package IBM SPSS Statistics version 21. We used the Chi-Square test to analyze categorical data and the independent-Sample T test to compare means. P-values of less than 0.05 were considered statistically significant. Only those hospital admissions were analyzed that both had a measurement moment 1 and 2.

RESULTS

Inclusion

There were 62 admissions of PD patients during the study period. 10 of those did not consent and we therefore excluded them.

MMSE measurements:

We were unable to obtain scores from 2 patients as they were in a poor physical condition and thus not able to do the tests. From another 8 patients we did not obtain a score at moment 2, because of discharge of these patients the same day or day after inclusion. So follow up MMSE data during admission were available from 42 admissions (31 different patients). Most of these (N=37, 88%) were included within the first 24 hours of hospitalization, 4 within 48 hours and one within 72 hours.

SCOPA-Cog measurements:

We were unable to obtain both moment 1 and 2 scores from 13 patients: 10 patients found this test too exhausting, 2 refused to do the test and for one patient there was no time left because of scheduled surgery. An additional 8 patients did not do the test at moment 2: 6 because of rapid discharge after inclusion and two because of refusal. In total we had SCOPA-COG data for both moment 1 and 2 for 31 admissions (24 different patients). These also had MMSE measurements for both moments.

PD and hospitalization related characteristics

Table 1 gives an overview of the general characteristics of the admitted PD patients. Almost two-third of the patients had an emergency admission. More than half of the included patients did undergo surgery, mainly under general anesthesia. At least half of the patients experienced complications during hospitalization. About 50% of those were delirium or confusion and about one-third infections. In about four tenths of the admissions there were medication errors.

Cognition

At the group level we found an overall slight improvement on the MMSE and SCOPA-Cog scales at discharge compared to admission. However a substantial part of the patients had cognitive decline during hospitalization: more than one fifth of the patients with the MMSE and more than a quarter of the patients with the SCOPA-Cog respectively on average 3.1 and 2.6 points (see Table 2).

PD medication errors and delirium or episode of confusion during hospitalization were the only significant risk factors for cognitive deterioration as measured with the MMSE at discharge compared to inclusion (see Table 3). For the SCOPA-Cog defined cognitive decline during admission, delirium/episode of confusion and longer duration of hospital stay were significant risk factors (see Table 4). For patients with delirium/episode of confusion during hospitalization, PD medication error is a significant risk factor (see Table 5).

In general patients with cognitive decline at discharge compared to admission had a longer mean length of hospitalization. For patients with a decrease in MMSE scores: 9.3 days (SD 6.4) compared to 8.9 days (SD 5.9), although this is not a significant difference: $p=0.86$.

Table 1. General, PD, and admission related characteristics

	MMSE ^a (n=42)	SCOPA-Cog ^a (n=31)
Male: %	52	58
Mean age: Years (SD)	73.7 (6.4)	73.3 (6.4)
Disease duration: Years (SD)	7.4 (6.8)	7.4 (7.4)
Hoehn and Yahr scale at admission: Stage (SD)	3.0 (1.0)	2.9 (0.9)
UPDRS-III score at admission: Score (SD) of total ^b (SD)	30.0 (11.7) of 101.1 (11.5)	29.2 (10.9) of 101.8 (9.9)
Reported memory complaints before admission: %	35.7	41.9
Patients with on-off periods: %	11.9	9.7
LED-value: mg/day (SD) at admission	538 (309)	554 (303)
PD medication:		
Levodopa: %	92.9	90.3
Dopamine agonist: %	47.6	58.1
Others: %	9.5	6.5
Not using PD medication: %	2.4	3.2
Higher LED-value at discharge: %	2.4	3.2
Lower LED-value at discharge: %	0	0
Number of patients with non per os	0	0
Hospitalization: Days (SD, minimum-maximum)	9.0 (6.0, 2-25)	9.6 (5.7, 2-23)
Medical specialism: %		
Orthopedics	23.8	25.8
Surgery	14.3	16.1
Cardiology	14.3	12.9
Internal medicine	11.9	12.9
Pulmonology	9.5	6.5
Gynecology	9.5	9.7
Neurology	7.1	9.7
Urology	7.1	6.5
Ophthalmology	2.4	0
Emergency admissions: %	64.3	61.3
Surgery: %	57.1	61.3
General anesthesia: % of surgeries	79.2	73.7
Local anesthesia: % of surgeries	20.8	26.3
Complications: % of all admissions	50.0	64.5
Delirium/episode of confusion	26.2	35.5
Infections	16.7	19.4
Urinary tract infection	9.5	12.9
Others: Each	2.4	3.2
Hallucinations	14.3	18.8
Decubitus	7.1	9.7
Hypotension	7.1	6.5
Others: Each	2.4	3.2
Fall incidences: %	4.8	6.5
PD medication error ^c : %	40.0	44.8
Wrong timing: % of medication error	75.0	69.2
Some rounds not distributed: % of medication error	56.3	53.8

Frequency to low: % of medication error	12.5	8.7
Opioid receptor agonist use during hospitalization	38.1	41.9
Contraindicated medication ^d :		
Metoclopramide: N prescribed, N administrated	2, 0	1, 0
Haloperidol: N prescribed, N administrated	1, 1	1, 1
Control of own PD medication: %	23.8	19.4
Involvement of paramedics:		
Physical therapy	47.6	54.8
Occupational therapy	4.8	6.5
Speech therapy	0	0
Involvement of PD nurse specialist: %	2.4	3.2

^a Only admissions having a second measurement (moment 2) were included.

^b Only those items of the UPDRS-III that could be measured both on moment 1 and 2 were included.

^c For one patient it was unclear if there was a medication error during admission and one patient didn't use PD medication.

^d No other dopamine antagonists, anti-emetics or atypical antipsychotics were prescribed.

Abbreviations: N: number, SD: standard deviation, LED: Levodopa Equivalent Dose, PD: Parkinson's disease.

Table 2. MMSE and SCOPA-Cog change during admission

	MMSE ^a	SCOPA-Cog ^a
Number	42	31
Admission: Score (SD) of total ^b (SD)	25.2 (4.7) of 29.4 (1.2)	19.9 (8.2) of 41.0 (5.5)
Discharge: Score (SD) of total ^b (SD)	25.5 (4.4) of 29.4 (1.2)	21.0 (8.8) of 41.0 (5.5)
Mean individual difference between measurement moment 1 and 2: Score (SD)	0.2 (3.1)	1.1 (3.3)
Deterioration: %, mean individual difference between measurement moment 1 and 2 (minimum, maximum)	21.4, 3.1 (-1, -14)	29.0, 2.6 (-1, -6)
No change: %, mean individual difference between measurement moment 1 and 2	45.2, 0.0	12.9, 0.0
Improvement: %, mean individual difference between measurement moment 1 and 2 (minimum, maximum)	33.3, 2.7 (1, 8)	58.1, 3.2 (1, 8)

^a Only admissions having a second measurement (moment 2) were included.

^b In some cases not all items could be analyzed because of patient related issues.

Abbreviations: SD: standard deviation, PD: Parkinson's disease.

Patients with a lower SCOPA-Cog test results compared to those who didn't, had significant longer average hospitalization duration i.e. 12.9 days (SD 6.5) compared to 8.3 days (SD 4.9): $p=0.04$. Patients with a delirium or episode of confusion were also admitted for longer periods: 10.3 to 8.6 days ($p=0.43$).

None of the PD patients who had been given control over their PD medication had a decreased MMSE score at discharge. Although these patients, compared to those without control over their medication, had a higher average MMSE score (respectively 26.3 to 24.7), and a lower average UPDRS-III score, 27.5 respectively 31.2, at admission (moment 1) there had been no significant difference in these variables: respectively $p=0.38$ and $p=0.40$. There

Table 3. MMSE and related factors

	Admissions (n) ^a	Lower MMSE score at discharge (n)	p-value ^b
Gender			
Male	22	7	0.14
Female	20	2	
Age ^c			
<75 years	23	6	0.48
≥75 years	19	3	
Disease duration ^{c,d}			
<8 years	31	5	0.19
≥8 years	10	4	
Reported memory complaints before admission			
No	27	5	0.70
Yes	15	4	
Patient with on-off periods			
No	37	8	1.00
Yes	5	1	
MMSE ^e < 25 at admission			
No	29	5	0.42
Yes	13	4	
Hoehn & Yahr at admission ^c			
stage <4	28	5	0.45
stage ≥4	14	4	
LED-value at admission ^c			
<700 mg/day	28	8	0.23
≥700 mg/day	14	1	
Admission duration ^c			
<10 days	29	6	1.00
≥10 days	13	3	
Emergency admission			
No	15	4	0.70
Yes	27	5	
Neurology department			
No	39	8	0.53
Yes	3	1	
Surgery			
No	18	3	0.71
Yes	24	6	
General anesthesia			
No	23	6	0.48
Yes	19	3	
Complications			
No	21	2	0.13
Yes	21	7	
Infections during hospitalization			
No	35	8	1.00
Yes	7	1	
Delirium/episode of confusion during admission			

No	31	3	0.005
Yes	11	6	
PD medication error ^a			0.004
No	24	1	
Yes	16	7	
Opioid receptor agonist use during hospitalization			0.27
No	26	4	
Yes	16	5	
Not in control of own PD medication ^f			0.08
No	10	0	
Yes	31	9	
Transfer to other department			0.66
No	34	8	
Yes	8	1	
Physical therapy during hospitalization			0.71
No	22	4	
Yes	20	5	
Overall	42	9	

^a Only admissions having a second measurement were included.

^b *P*-value <0.05 is considered significant.

^c Both higher and lower cut of points were analyzed but *p*-values were not significant.

^d For one patient there is an unknown disease duration. As such, 41 patients were included.

^e For one patient it was unclear if there was a medication error during admission and one patient didn't use PD medication.

^f One patient didn't use PD medication.

Chi-Square test was used.

Abbreviations: N: number, LED: Levodopa equivalent dose, PD: Parkinson's disease.

were less medication errors in this group ($p=0.003$), but no other significant differences for the variables in table 4. One patient in control of his PD medication had SCOPA-Cog tested at moment 1 and 2 and had a cognitive decline of one point.

Of the 9 patients with a decreased SCOPA-Cog score at discharge, just 4 also had a decrease in MMSE score. The other 5 patients with a decrease of the SCOPA-Cog test results, MMSE did not change (comparing moment 1 and 2). When comparing those patients with both worsening of MMSE and SCOPA-Cog ($N=4$) to those not having any worsening on one of the tests ($N=18$), delirium or episode of confusion during hospitalization was the only significant risk factor for worsening of cognition at discharge compared to admission ($p=0.01$). These deteriorating patients were also admitted for a longer period, but this was not statistically significant 14.3 compared to 8.8 days ($p=0.09$).

Table 4. SCOPA-Cog and related factors

	Admissions (n) ^a	Lower SCOPA-Cog score at discharge (n)	p-value ^b
Gender			
Male	18	7	0.24
Female	13	2	
Age ^c			
<75 years	19	7	0.42
≥75 years	12	2	
Disease duration ^{c,d}			
<8 years	23	6	0.64
≥8 years	7	3	
Reported memory complaints before admission			
No	18	6	0.70
Yes	13	3	
Patient with on-off periods			
No	28	7	0.20
Yes	3	2	
SCOPA-Cog < 20 at admission ^c			
No	17	4	0.15
Yes	14	7	
Hoehn & Yahr at admission ^c			
stage <4	22	4	0.08
stage ≥4	9	5	
LED-value at admission ^c			
<700 mg/day	20	7	0.43
≥700 mg/day	11	2	
Admission duration ^c			
<10 days	20	3	0.04
≥10 days	11	6	
Emergency admission			
No	12	5	0.20
Yes	19	4	
Neurology department			
No	28	8	1.00
Yes	3	1	
Surgery			
No	12	3	1.00
Yes	19	6	
General anesthesia			
No	17	6	0.46
Yes	14	3	
Complications			
No	11	1	0.11
Yes	20	8	
Infections during hospitalization			
No	25	6	0.32
Yes	6	3	
Delirium/episode of confusion during admission			

No	20	2	0.003
Yes	11	7	
PD medication error ^e			0.09
No	16	2	
Yes	13	6	
Opioid receptor agonist use during hospitalization			0.43
No	18	4	
Yes	13	5	
Not in control of own PD medication ^f			0.64
No	6	1	
Yes	24	8	
Transfer to other department			0.61
No	26	7	
Yes	5	2	
Physical therapy during hospitalization			0.13
No	14	2	
Yes	17	7	
Overall	31	9	

^a Only admissions having a second measurement were included.

^b *P*-value <0.05 is considered significant.

^c Both higher and lower cut of points were analyzed but *p*-values were not significant.

^d For one patient there is an unknown disease duration. As such, 41 patients were included.

^e For one patient it was unclear if there was a medication error during admission and one patient didn't use PD medication.

^f One patient didn't use PD medication.

Chi-Square test was used.

Abbreviations: N: number, LED: Levodopa equivalent dose, PD: Parkinson's disease.

Table 5. Delirium/confusion during hospitalization and related factors

	Admissions (n) ^a	Delirium/confusion during hospitalization (n)	p-value ^b
Gender			
Male	22	8	0.116
Female	20	3	
Age ^c			
<75 years	23	7	0.73
≥75 years	19	4	
Disease duration ^{c,d}			
<8 years	31	6	0.10
≥8 years	10	5	
Reported memory complaints before admission			
No	27	8	0.72
Yes	15	3	
Patient with on-off periods			
No	37	9	0.59
Yes	5	2	
MMSE ^c < 25 at admission			
No	29	7	0.71
Yes	13	4	
Hoehn & Yahr at admission ^c			
stage <4	28	8	0.72
stage ≥4	14	3	
LED-value at admission ^c			
<700 mg/day	28	9	0.28
≥700 mg/day	14	2	
Admission duration ^c			
<10 days	29	7	0.71
≥10 days	13	4	
Emergency admission			
No	15	6	0.16
Yes	27	5	
Neurology department			
No	39	11	0.55
Yes	3	0	
Surgery			
No	18	2	0.08
Yes	24	9	
General anesthesia			
No	23	5	0.50
Yes	19	6	
Infections during hospitalization			
No	35	8	0.35
Yes	7	3	
PD medication error ^a			
No	24	2	0.007
Yes	16	8	
Opioid receptor agonist use during hospitalization			

No	26	4	0.07
Yes	16	7	
Not in control of own PD medication ^f			0.24
No	10	1	
Yes	31	10	
Physical therapy during hospitalization			0.22
No	22	4	
Yes	20	7	
Overall	42	11	

^a Only admissions having a second MMSE measurement were included.

^b *P*-value <0.05 is considered significant.

^c Both higher and lower cut of points were analyzed but *p*-values were not significant.

^d For one patient there is an unknown disease duration. As such, 41 patients were included.

^e For one patient it was unclear if there was a medication error during admission and one patient didn't use PD medication.

^f One patient didn't use PD medication.

Chi-Square test was used.

Abbreviations: N, number; LED, Levodopa equivalent dose; PD, Parkinson's disease.

DISCUSSION

We had previously reported that a substantial part of PD patients have motor function deterioration during hospitalization.^{7,8} We have now made similar observations for cognitive functioning as well. We documented this prospectively with both MMSE and SCOPA-COG assessments in 42 PD patients admitted to a general hospital for varying reasons. Cognitive deterioration was more pronounced when measured with the SCOPA-Cog (29%) than with the MMSE (21%), although we were not able to take both test in all patients.

Our study has limitations. The study population is small, so the results should be interpreted cautiously. There are also some inherent possible biases in neuropsychological testing of hospitalized patients. Fatigue and physical condition might have impacted performance negatively. A substantial portion of PD patients found the SCOPA-Cog too exhausting and did thus not complete both tests. MMSE, on the other hand, may not be sensitive enough to detect mild (changes in) cognitive impairments.¹³⁻¹⁸ As the interval between the two tests was relatively small, there could have been a learning effect influencing the cognitive evaluations. We were also not able to definitively rule out delirium or episodic confusion at the time of the tests: since this was an observational study trying not to influence daily practice, we had not asked the treating physicians explicitly to do tests for delirium. Finally, pre-existing neuropsychological impairments might also have affected our study, but, since most patients had never been tested, we do not have data on this.

This is however the first prospective study with 2 different validated neuropsychological tests taken at two different time points during hospitalization, and it shows that an important

portion of hospitalized PD patients experiences cognitive deterioration. This study supports, as shown in previous studies, the high rate of delirium during hospitalization and related increased length of hospital stay and therefore does confirm that this is an important clinical problem.^{11,19,20} However, since the included PD patients were not compared with patients without PD we are not able to conclude that PD patients are more vulnerable for cognitive deterioration during hospitalization than patients without PD.

There are a number of possible causes and risk factors for the cognitive worsening that we found in our study. Delirium or episode of confusion during hospitalization was a significant risk factor for a worse test result on both the MMSE and SCOPA-Cog at the end of hospitalization. This agrees with previous reports that delirium can have a prolonged effect and symptoms can persist after discharge.^{10,11,19,20} PD medication errors during hospitalization are frequent and we found they were also a significant risk factor for cognitive decline as measured with the MMSE. Duration of the admission was a risk factor for cognitive deterioration as measured with the SCOPA-Cog. In general, patients worsening on the MMSE (not significant) and SCOPA-Cog (significant) had longer mean length of hospitalization. There may be a causative relation between the two, but the direction of this relation might work both ways.

The same holds true for delirium and medication errors. Medication errors during hospitalization are an important risk factor for PD patients to develop delirium or confusion. On the other hand PD medication errors could also be the result of cognitive impairment, although our overall impression during the almost daily visits was that the latter was less important.

Interventions to prevent delirium in hospitalized PD patients are important, but evidence for their effects are scarce.²¹ Based on our study we think an important area of possible improvement is medication errors. Preventing PD medication errors could be an important step in preventing worsening of cognitive function during hospitalization for PD patients, including associated delirium. We found that none of the patients who continued to take their medication themselves had worse MMSE final test results. This could be due to confounding, but we feel that there is enough evidence here to justify a randomized trial studying the effect of autonomous medication scheduling by the hospitalized PD patient.

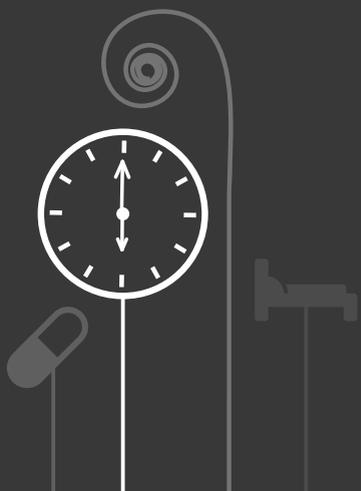
CONCLUSION

The main finding of this study is that there is a substantial part of the hospitalized PD patients that have cognitive deterioration at discharge mainly caused by delirium or episode of confusion during hospitalization resulting in a longer mean length of hospitalization. Measurements should be taken to prevent delirium and since PD medication errors seem to play an important role this should be prevented.

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A stylized white line-art illustration on a dark background. It features a clock face with a vertical arrow pointing up and down, a pill, and a stethoscope.

CHAPTER 6

PARKINSON'S DISEASE AND HOSPITALIZATION: THE NEED FOR GUIDELINES

Main results covered in this chapter have been published
as letter to the editor:
O.H.H. Gerlach, V.J.H. Rouvroije, W.E.J. Weber.

Parkinsonism and Related Disorders 2011;17:498.

ABSTRACT

Introduction

During hospitalization Parkinson patients have a higher morbidity and mortality, and a longer hospital stay compared with controls. We analyzed whether or not hospitalized PD patients are cared for with extra attention and if there are guidelines that are generally used in daily practice.

Methods

A questionnaire was sent to all hospitals in the Netherlands, addressed to a neurologist with special expertise on movement disorders or, if not present, a random neurologist was chosen. Questions were related to general hospital related aspects, care by a neurologist during the hospitalization of PD patients, and perioperative care.

Results

A total of 94 questionnaires were sent with a response rate of 60%. In only 2 hospitals the neurologist is consulted for every admitted Parkinson's disease patient. In the other clinics Parkinson's patients are mainly visited on specific request of treating physician or of the hospitalized patient. In 75% of the hospitals there is no system to trace admitted patients. In 11% of the hospitals the movement disorder specialist is involved during the perioperative period of a PD patient, otherwise only on request when the treating specialist expects complications or when complications have already occurred. In just 2 hospitals is a protocol available with regard to the perioperative period. In 75% of the hospitals is a PD nurse specialists present. In 48% of these hospitals, they are not involved in the treatment during the hospitalization of PD patients.

Conclusions

In many hospitals during hospitalization PD patients are not cared for with extra attention by a movement disorder team. To provide the necessary extra care for every hospitalized PD patients a written multidisciplinary protocol could be useful.

INTRODUCTION

Parkinson's disease (PD) patients are vulnerable because of both motor and non-motor symptoms and age related comorbidity.¹⁻³ During hospitalization Parkinson patients have a higher morbidity and mortality, and a longer hospital stay, compared with controls.^{4,5} One of the key problems seems to be the lack of adherence to precise medication schedules and lack of knowledge as to anti-Parkinson drugs and their interactions.⁵⁻⁸ Standard consultation by a neurologist may improve the care for these patients.⁹ Guidelines could help to improve delivered care. It is however unclear if PD patients receive extra attention during hospitalization.

In this chapter we therefore analyzed whether PD patients are cared for with extra attention when they are admitted into a hospital, and if there were guidelines present that are generally used in daily practice.

METHODS

We mailed a questionnaire to all hospitals in the Netherlands (see additional file 4). This questionnaire was addressed to a neurologist with special expertise on movement disorders or, when there was no neurologist with this area of interest, a random neurologist was chosen. The neurologist was asked to return the questionnaire or answer the questions on the Internet. After a few weeks a reminder was sent to those that didn't respond. Questions were about general aspects related to the hospital and neurology department, the involvement of neurology during the hospitalization of PD patients for a specialty other than neurology, and perioperative care. The statistical analyses are performed with PASW-version 18.0 (SPSS, Chicago).

RESULTS

Response rate

A total of 94 questionnaires were sent. The response rate was 60%: 5 out of 8 (63%) for university hospitals and 51 out of 86 (59%) for non-university hospitals. Half of the responders were neurologists with special expertise on movement disorders.

Neurology department

There were on average 6.9 neurologists per hospital (full-time equivalent 2.5 till 15). Total number of known PD patients per hospital did vary from 10 till more than 500.

There is a Parkinson's disease nurse specialist available in 75% of the clinics (n=42).

Hospital related PD care

General

In 2 hospitals there is neurological consultation for every admitted Parkinson's disease patient. In the other clinics Parkinson's patients are mainly visited on specific request of the treating specialist (86%) and/or on specific request of the hospitalized patient (18%).

In 75% of the hospitals there was no system to trace admitted Parkinson's disease patients by the movement disorder specialist. In most other hospitals PD patients are asked to inform the treating doctor to consult neurology when hospitalized. No neurologist reports an automated warning system to alert the movement disorder team that a new PD patient is hospitalized.

In 64% of the hospitals there is no medication list available that shows interaction between different types of medication with PD medication.

Perioperative care

In 11% of the hospitals (all non-university ones) the movement disorder specialist is involved during every surgery of a PD patient, otherwise only on request when the treating specialist expects complications or when complications have already occurred. In half of the clinics no parenteral dopaminergic medication is used perioperatively. In just 2 hospitals there is a protocol available with regard to the perioperative period. This concerns advice about medication.

For both perioperative and postoperative complications most frequent ones seen by the movement disorder specialist are delirium, followed by motor problems, and other cognitive problems.

PD nurse specialist

PD nurse specialists are not involved during the hospitalization of patients with PD in 48% of the hospitals that have a PD nurse specialist. Of those clinics that have a nurse specialist, neurologists believe that because of the PD nurse specialist there are less Parkinson patients admitted to the neurology department and other departments in 40% and 17% of the hospitals respectively.

DISCUSSION

PD patients are vulnerable especially during hospitalization and therefore might need extra care.^{4,5} There is some evidence that a PD patient can benefit from an early neurological consultation and overall a multidisciplinary approach seems desirable.^{4,5,9} However, data

presented in this chapter shows that in most hospitals admitted PD patients, whether or not having surgery, are just visited by the movement disorder team on special request of the treating specialist or PD patient. This might result in late consultation and these patients therefore may not have the advantage of multidisciplinary management. Although in most hospitals there is a PD nurse specialist, in the majority of the hospitals these were not involved in the care to the hospitalized PD patient.

A problem seems to be that there is no warning system that alerts the movement disorder team of newly admitted PD patients. As such, a proactive approach from this team is difficult. Just 2 hospitals in the Netherlands reported of a protocol concerning the preoperative period.

There are some limitations to the study. Unfortunately not all hospitals did reply the questionnaire, so we could have missed hospitals that have systems to trace new hospitalized PD patients and have written protocols. We were not able to analyze why the PD nurse specialist in many hospitals is not involved with the care for admitted PD patients. Maybe part-time jobs and busy schedules play a role.

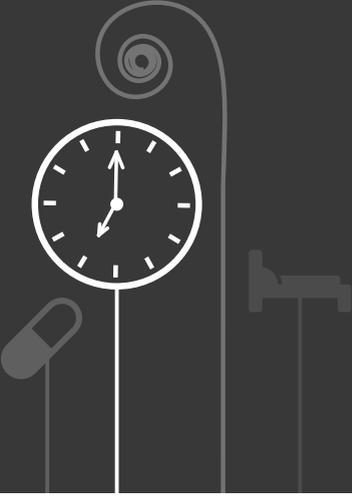
However we believe that this study supports the need for a written protocol and extra attention to the specific problems Parkinson's patients face when admitted to a hospital.

CONCLUSIONS

During hospitalization in many hospitals PD patients are not cared for with extra attention by a movement disorder team. There is still much room for improvement. To provide the necessary extra care for every hospitalized PD patients a written multidisciplinary protocol could be useful.

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CHAPTER 7

GENERAL DISCUSSION

INTRODUCTION

Parkinson's disease (PD) is a common neurologic disorder mainly affecting the elderly.^{1,2} PD is a progressive neurodegenerative disorder which has great influence on the patients' quality of life.^{3,4} Next to this, PD has both major social and economic implications.⁵⁻⁸ The objective of the studies reported in the present thesis was to examine the problems hospitalized PD patients encounter in order to delineate ways and/or tools to improve the quality of care. Therefore, the first aim was to explore what is known about the extent of problems and related possible solutions (*Chapter 2*). To further investigate deterioration of Parkinson's disease symptoms during hospitalization, we evaluated the prevalence and risk factors of deterioration including all wards. This was first done retrospectively, (*Chapter 3*) and secondly, prospectively, (*Chapter 4*) with the focus on motor symptoms. However, since non-motor symptoms contribute to disability and impaired quality of life with cognitive impairment as one of the most invalidating non-motor symptom,⁹⁻¹² we also aimed to assess cognitive decline prospectively (*Chapter 5*). Next, we analyzed if PD patients are cared for with extra attention during hospitalization (*Chapter 6*).

In this general discussion I will focus on three main topics. I will discuss what the results of this thesis have added to the existing literature, and place these in a broader perspective.

These three topics are:

- Hospitalization and adverse events
- Medication errors
- Healthcare paradox

Also, I will discuss general limitations of this thesis, its implications, and perspectives for further research.

HOSPITALIZATION AND ADVERSE EVENTS

Adverse events during the overall hospitalization of specific patient groups, as PD patients, have not been studied systematically. So the aim of this thesis was to analyze the problems PD patients are confronted with during hospitalization.

What we learned

In general, PD patients are hospitalized longer and have more complications than comparable control groups (*Chapter 2*). Infections and confusion are the most common complications, whether or not patients are having surgery (*Chapter 2,3,4*). Both deterioration of motor and cognitive functions are more specific PD-related complications and have been reported during hospitalization in some retrospective studies (*Chapter 2*). We were

the first to systematically analyze proportions, reasons, and severity of deterioration, both retrospective and prospective, with the focus not only on Accident & Emergency departments and surgical wards, but also on other wards (*Chapter 3,4,5*). There is motor function deterioration in a substantial number of the admitted PD patients (*Chapter 3,4*). The most important hospitalization related risk factor for this deterioration was incorrect PD medication administration, followed by infections during hospitalization (*Chapter 3,4*). Both aspects have been attributed to motor exacerbations.¹³ In accordance with this, we found that many PD patients had a substantially worse cognitive function at discharge (*Chapter 5*). An episode of confusion (whether or not delirium) during hospitalization was the most important risk factor for cognitive deterioration at discharge (*Chapter 5*). Again, PD medication errors are an important factor for deterioration, as it is both a significant risk factor for deterioration as measured with the MMSE and for an episode of confusion during hospitalization (*Chapter 5*). Patients that had control of their own PD medication didn't show motor function deterioration and had less cognitive function deterioration (*Chapter 4,5*).

Broader perspective

Some patients are more at risk for adverse events than others.^{14,15} In general, different specialties and departments show higher rates, especially specialties involving surgery.^{14,16} Also, age seems important since the older the patient, the higher the rates of adverse events.¹⁴⁻¹⁸ For the elderly, most adverse events are more common, and the negative effects can be more severe.^{15,18} Drug and surgery related complications are the most common types.^{15,18} Important factors for this are the higher rate of complicated diseases and comorbidity for this older patient group, and the skills of caregivers to apply the existing knowledge to more complex situations.^{15,18}

An important associated factor for hospital encounters of PD patients is the number of comorbidities.¹⁹ These, in combination with the complexity of PD itself, with its vulnerable PD medication schedule and the average higher age, makes this patient group prone for adverse events. Since PD medication errors during hospitalization are not caused by the underlying disease but by the treatment team and result in patients with PD related disability, this can be seen as adverse events and should be classified as preventable. With the aging of the population and therefore the growing number of hospitalized PD patients, the awareness and prevention of adverse events for this specific population are becoming more important.¹⁸

MEDICATION ERRORS

As shown before, medication errors are frequent adverse events. In this thesis we aimed to analyze the extent this problem for hospitalized PD patients.

What we learned

We found that many PD patients are exposed to PD medication errors and administration of antidopaminergic drugs during admission (*Chapter 2*). PD patients did confirm this high rate of nonadherence to PD medication schedules as they reported this problem in 26% of the admissions (*Chapter 3*). Our observations in *Chapter 4* showed even higher rates of PD medication problems, namely in 39% of the cases. Our results didn't support the recently reported high rate of inappropriate antidopaminergic drugs prescription and administration, but did confirm existence of this problem (*Chapter 4*).^{20,21} These findings do agree with the high rates of adverse medication errors and support the necessary continuing awareness and attention for medication errors in general, and more specific, for medication related to PD during the hospitalization of this distinct, vulnerable patient group.

Broader perspective

Although the focus in this thesis is on PD patients, the problem of medication errors concerns all hospitalized patients in different departments.²²⁻²⁴ Especially older patients seem to have a high risk for errors because of comorbidities and polypharmacy.^{20,25,26} Medication reconciliation, i.e. identifying of the most accurate medication list across the healthcare setting is important to prevent harm to the patient.^{25,27,28} Pinpointing the correct medication list however, can be a time consuming challenge because of poor self-reporting of prescribed medication and poor compliance.^{25,28,29}

Changes of environment or healthcare levels of a patient can result in unwanted changes or discontinuing of medication regimes, especially around hospitalization.^{27,29,30} Both admission to and discharge from the hospital are vulnerable moments for unintended changes in medication schedules and can harm the patient.²⁷⁻³⁰ Intervention studies have shown positive results in improving medication discrepancies for both moments, although the effects on patients' disability are not clear.³⁰ There seems to be an important role for the pharmacist in coordinating and controlling patients' medication.^{27,30} Also, patient counseling and education before and after discharge can have positive results, and there might be a role for information technology.³⁰

To prevent PD medication errors during hospitalization an in-patient PD unit with a specially trained treatment team could be an option.³¹

HEALTHCARE PARADOX

Quality and safety of health care has received much more attention in recent years. Nevertheless, during hospitalization adverse events are common. At first glance, the aim of decreasing healthcare costs may contrast the possibility of offering better quality of care. Paradoxically, less money might result in better care.

What we learned

There are high complication rates and adverse events during the hospitalization of PD patients (*Chapter 2,3,4,5*). In most hospitals, PD patients are not treated with extra attention, despite the vulnerability of this specific patient group (*Chapter 6*). As a result, curing and harming the patient can coexist. Therefore, for the specific group of patients studied in this thesis, the hospitalized PD patient, there seems to be room for improvement which could result in better quality of care, a higher efficiency rate and lower costs. There are high rates of emergency visits and hospitalization rates per year (*Chapter 2,3*).¹⁹ The high number of admissions combined with average admission duration highlight that at any given time, in an average sized hospital, there is most likely a PD patient hospitalized (*Chapter 3,4*). Therefore, there should be a daily focus on this problem.

Broader perspective

Healthcare organizations have to meet increasing performance indicators. Total PD related direct and indirect costs are expected to increase as the size of the elderly population, and therefore the number of PD patients, grows.⁵⁻⁸ Financial resources are limited, however. Decision making is more and more based on cost-effectiveness studies, especially in chronic diseases such as PD.³² Limited available financial resources can result in a more critical look at conventional delivered care and might lead to novel ways to improve current care. This optimization of care might have a positive effect on relieving healthcare burden and quality of care and life. Prior studies have shown that changes in daily practice by healthcare providers can result in substantial cost reduction without negatively affecting patients' satisfaction while improving the quality of delivered care.^{33,34} The paradoxical effect of decreasing healthcare costs might be better quality of care.

LIMITATIONS OF THE THESIS

There are limitations that could have influenced the outcomes. In both the retrospective and prospective study, there are relatively small numbers of hospitalized PD patients. The results presented in the retrospective study could have been influenced by recall bias, and there might have been observation bias in the prospective study since the observations were not blinded. We may have missed some admissions and not all patients gave informed consent. This could have caused selection bias. In the prospective study, not all patients were included immediately after admission, and therefore this vulnerable moment for medication errors³⁵ was not analyzed properly. Next to this, the self-report of home PD medication schedules and preexistent motor and neuropsychological functions before admission was not objectified. During the admissions, the treating physicians did not analyze delirium structurally, and therefore there was no clear distinction between an episode of confusion

or delirium. However, since the problems PD patients encounter when admitted to the hospital, as presented in the systematic review (*Chapter 2*), do agree with results from the retrospective multicenter study (*Chapter 3*) and the single center prospective study, (*Chapter 4,5*) and data presented in *Chapter 3* are confirmed by the results in *Chapter 4*, we believe the study results are generalizable and do not invalidate our conclusions.

IMPLICATIONS AND FUTURE PERSPECTIVES

Implications

First of all, if possible, hospitalization should be prevented. Close monitoring of the patient at the neurologist outpatient clinic and in its own environment, preferably in a multidisciplinary setting, could be helpful.^{19,36,37} When hospitalized, every PD patient should receive full attention (independent of admitted department or whether or not having surgery). Because of the vulnerability of PD patients and the unfamiliarity with PD of many treating physicians, the approach should be multidisciplinary from the moment of admission. Next to the treating team, neurology and/or geriatrics should be included in this multidisciplinary team. Since most hospitals have a PD nurse specialist (*Chapter 6*), they could have a coordinating and monitoring role. Special attention should be paid to personal PD medication regimes since this should be administrated as the home schedule. Self-administration of PD drugs could be considered when possible. There could be a role for a clinical pharmacist in controlling correct copying of home schedules and distribution of PD medication. Next to this, extra attention should be given to prevention and quick recognition of complications such as infections and episodes of confusion or delirium. Since every physician or nurse working in a hospital has to deal with PD patients, these suggestions should be included in a hospital-wide protocol. The execution of the protocol could be supported additionally by education of hospital employees and PD patients and an (computerized) alert system to trace admitted PD patients. Another option could be the introduction of a specialist in-patient PD unit for every hospitalized PD patient, since a recent study showed positive effects on PD medication errors and length of stay.³¹

Future perspectives

Although there is increased attention for the problems the PD patient face when hospitalized, the positive effect of recommended interventions is not yet proven. Therefore, future studies should be taken to shed more light on these aspects. Preferably, this would be a multi-center prospective placebo-controlled randomized trial with sufficient number of patients, with the focus on both motor and non-symptoms. An in-patient PD unit could be the starting point.

CONCLUSION

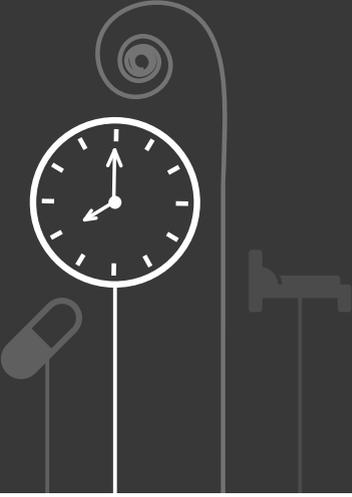
In conclusion, PD patients are hospitalized more frequently and generally longer than non-PD patients. During hospitalization, there is an increased complication rate of mainly infections and confusion. Many hospitalized PD patients have motor and cognitive function deterioration at discharge. The most important reasons for this are PD medication errors, confusion during hospitalization and infections. Measurements should be taken to prevent adverse events and improve care, preferably incorporated in a hospital-wide protocol, and future research should focus on analyzing the effects of these interventions.

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CHAPTER 8

SUMMARY

Parkinson's disease (PD) is a progressive neurodegenerative disease that has major impact on the quality of life. The social and economic impacts are substantial. PD patients do have a high healthcare consumption rate, and the risk of hospitalization is high. During hospitalization, this vulnerable patient group is at risk for complications and other adverse events. In this thesis we studied the spectrum of problems patients with PD encounter during hospitalizations and explored those aspects that can be changed to improve quality of care.

Chapter 1 provides a general background of PD: Next to epidemiology, pathogenesis, the clinical diagnosis, the diverse symptoms, treatment options, and the different aspects that influence the quality of life are discussed. Subsequently, the high use of healthcare facilities by PD patients and related costs are described. More in detail, adverse events and the Dutch situation concerning the hospitalization of this vulnerable patient group are emphasized.

Chapter 2 describes the results of a systematic review of the literature concerning hospitalization of PD patients. The main findings of this review are that PD patients have more emergency room encounters and are hospitalized more frequently than non-PD patients. They are hospitalized because of direct and indirect disease related morbidity and non-PD related causes. Also, the duration of hospitalization is generally longer and there are more complications during these admissions. There is a high risk for infections, confusion, decubitus, and falls, and there are indications that there is a high rate of PD medication errors. There are many unresearched recommendations concerning the improvement of care for inpatient PD patients. There are just a few studies on medication continuation during surgery and one study analyzing the effect of neurologic consultation. Overall, most studies were retrospective, had small patient numbers and were related to admissions of PD patients having surgery.

In *Chapter 3* we focused on the deterioration of motor function of PD patients during hospitalization. In this retrospective study, PD patients from three different hospitals were asked to answer a standardized questionnaire concerning a possible hospitalization in the last year. One third of the patients had one or more complications. One fifth of the cases reported deterioration of motor function during hospitalization. In the clinical files there was an underreporting of this PD deterioration. In a quarter of the admissions there were PD medication errors, and for this variable there was no significant difference between admission to a neurological or other ward or whether or not having surgery. The most important risk factor for motor function deterioration during hospitalization was PD medication errors followed by infections and a higher levodopa equivalent dose per day.

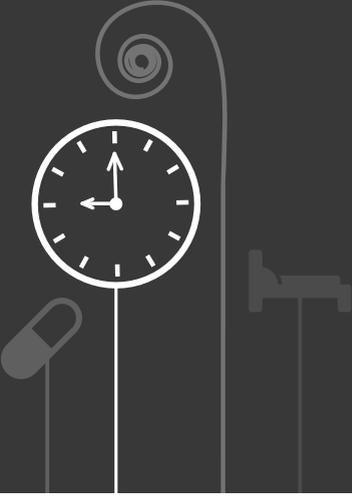
In *Chapter 4* we investigated the motor function outcomes during hospitalization prospectively. Different variables were analyzed to find possible factors that could cause

motor function deterioration. There was a clinically important worsening of motor function at discharge in more than one quarter of the admissions. During almost half of the admissions, there were complications, mainly confusion and infections. There were PD medication errors in almost four tenth of the admissions, resulting in longer (but not statistically significant) average admission duration. This last factor is the most important risk factor for motor function deterioration at discharge, followed by infections during hospitalization. None of the PD patients that had control of their own PD medication had motor function deterioration.

Since cognitive impairment is one of the most invalidating non-motor symptoms, in *Chapter 5* we additionally prospectively analyzed cognitive functions during the hospitalization of PD patients using different cognitive function tests. There was cognitive deterioration at discharge in about a quarter of the admissions (a little less or more depending on the test that was used). An episode of confusion or delirium, occurring in more than a quarter of the admissions is a significant risk factor for cognitive deterioration at discharge, and PD medication errors during hospitalization are related to an episode of confusion or delirium. Patients that deteriorated were admitted on average longer, however this was not statistically significant.

In *Chapter 6* we explored whether PD patients are cared for with extra attention by the treating team during hospitalization as per the higher complication risk. With the help of a questionnaire, we inventoried the care during hospitalization. In most hospitals in the Netherlands, there is no protocol available concerning the hospitalized PD patients. Neurological consultations are by specific request of the treating specialist. Although in most hospitals there is a PD nurse specialist available, in half of the hospitals they are not involved during the hospitalization of PD patients.

In *Chapter 7*, a general discussion of the main findings is given and placed in a broader perspective. This is followed by recommendations for improvement of care and for directions for future research. The chapter ends with concluding remarks.



CHAPTER 9

NEDERLANDSE SAMENVATTING
SUMMARY IN DUTCH

De ziekte van Parkinson (ZvP) is een neurodegeneratieve aandoening met grote invloed op de kwaliteit van het leven. Daarnaast heeft deze ziekte een grote sociale en economische impact. Mensen met deze ziekte maken veel gebruik van gezondheidszorgvoorzieningen en hun kans op een ziekenhuisopname is groot. Tijdens een ziekenhuisopname loopt deze kwetsbare patiënten populatie een groot risico op complicaties en andere ongewenste gebeurtenissen. In dit proefschrift beschrijven we de verschillende problemen waar patiënten met de ZvP tijdens ziekenhuisopname mee geconfronteerd worden en maken we die aspecten inzichtelijk die tot een verbetering van de kwaliteit van zorg kunnen leiden.

In *Hoofdstuk 1* wordt een algemeen overzicht gegeven over de ZvP: Naast epidemiologie, pathogenese, de klinische diagnose, de verschillende klinische symptomen en behandelingen, worden de verschillende aspecten die van invloed zijn op de kwaliteit van leven vermeld. Vervolgens komen het grote gebruik van gezondheidszorgvoorzieningen door patiënten met de ZvP en gerelateerde kosten aan bod. Meer in detail worden problemen tijdens ziekenhuisopname en de Nederlandse situatie met betrekking tot deze kwetsbare patiënten groep belicht.

In *Hoofdstuk 2* worden de bevindingen van een systematisch overzicht van de bestaande literatuur over de hospitalisatie van Parkinsonpatiënten weergegeven. Patiënten met de ZvP bezoeken de spoedeisende hulp vaker en worden vaker opgenomen in het ziekenhuis dan patiënten die deze aandoening niet hebben. Oorzaken voor ziekenhuisopnames zijn zowel direct als indirect met de ziekte gerelateerde comorbiditeit als oorzaken die los staan van deze aandoening. De ziekenhuisopnames zijn over het algemeen langer en er zijn meer complicaties. Er is een hoog risico op infecties, verwardheid, decubitus en valpartijen en er zijn aanwijzingen dat er veel met de ZvP gerelateerde medicatie fouten worden gemaakt. Er zijn veel niet wetenschappelijk onderzochte adviezen met betrekking tot het verbeteren van de zorg beschreven. Er zijn slechts enkele studies die het continueren van ZvP gerelateerde medicatie beschrijven tijdens een operatie en er is één studie die kijkt naar het effect van een neurologische consultatie. Over het algemeen waren de meeste studies retrospectief, was er slecht kleine aantal patiënten geïncludeerd en hadden de meeste artikelen betrekking op ziekenhuisopnames van patiënten die een operatie ondergingen.

In *Hoofdstuk 3* onderzochten we het beloop van de motorische symptomen van patiënten met de ZvP tijdens een ziekenhuisopname. In deze retrospectieve studie is aan patiënten met de ZvP van drie verschillende ziekenhuizen gevraagd een gestandaardiseerde vragenlijst in te vullen die betrekking had op een mogelijk ziekenhuisopname in het voorafgaande jaar. Eén derde van de patiënten gaf aan één of meer complicaties gehad te hebben. Eén vijfde melde motorische verslechtering tijdens ziekenhuisopname. In de klinische dossiers was er een onderrapportage van deze verslechtering. Tijdens een kwart van de opnames waren er met de ZvP gerelateerde medicatie fouten. Er was voor deze variabele geen

significants verschil was tussen neurologische en niet neurologische afdelingen en ook niet voor patiënten die wel of geen operatie hebben gehad. De belangrijkste risicofactor voor motorische verslechtering tijdens ziekenhuisopname was ZvP gerelateerde medicatie fouten, gevolgd door infecties en een hogere levodopa equivalente dosis per dag.

In *Hoofdstuk 4* werd het beloop van de motorische functie van patiënten met de ZvP gedurende een ziekenhuisopname prospectief geanalyseerd. Verschillende variabelen zijn bekeken om er achter te komen welke de oorzaak zouden kunnen zijn voor motorische verslechtering. In meer dan een kwart van de ziekenhuisopnames was er een klinisch relevante motorische verslechtering bij ontslag. Gedurende bijna de helft van de opnames waren er complicaties, vooral verwardheid en infecties. In viertiende deel van de ziekenhuisopnames waren er ZvP gerelateerde medicatie fouten. Dit resulteerde in langere ziekenhuisopnames alhoewel het verschil niet significant was. ZvP gerelateerde medicatie fouten was de belangrijkste risicofactor voor een slechtere motorische functie bij ontslag, gevolgd door infecties tijdens opname. Van alle patiënten die ZvP gerelateerde medicatie in eigen beheer hadden, had er geen een motorische verslechtering.

In *Hoofdstuk 5* werd vervolgens prospectief gekeken naar de cognitieve functies van Parkinsonpatiënten tijdens de ziekenhuisopnames. Hierbij is gebruik gemaakt van verschillende cognitieve testen. In ongeveer een kwart (afhankelijk van de gebruikte test wat meer of minder) van de opnames was er een cognitieve verslechtering bij ontslag. Een periode van verwardheid of delirium tijdens opname kwam voor in meer dan een kwart van de opnames. Dit is een significante risicofactor voor cognitieve verslechtering bij ontslag. ZvP gerelateerde medicatie fouten is gerelateerd aan een periode van verwardheid of delirium. De patiënten die verslechterde hadden gemiddeld langere ziekenhuisopnames (niet significant).

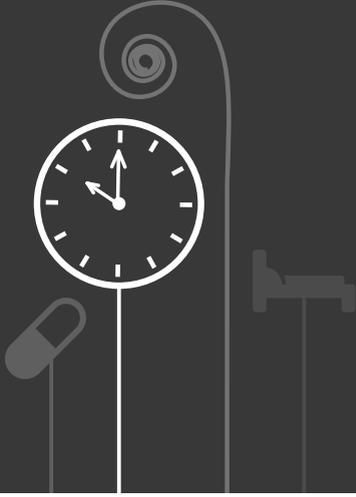
In *Hoofdstuk 6* hebben we gekeken of patiënten met de ZvP van het behandelteam extra aandacht krijgen tijdens een ziekenhuisopname gezien het hogere complicatierisico. Met een vragenlijst inventariseerden we de zorg voor deze patiënten tijdens een ziekenhuisopname. Het bleek dat in de meeste Nederlandse ziekenhuizen geen protocol beschikbaar was waarin de zorg beschreven werd die betrekking heeft op de in een ziekenhuis opgenomen Parkinsonpatiënt. Ook bleek de neuroloog in de meeste ziekenhuizen niet standaard bij iedere patiënt met de ZvP in medebehandeling was. Dit gebeurde meestal pas na specifiek verzoek van de hoofdbehandelaar. Alhoewel er in de meeste ziekenhuizen een Parkinsonverpleegkundige werkzaam is, zijn deze in de helft van de gevallen niet betrokken bij zorg gedurende de opname.

In hoofdstuk 7 wordt een algemene discussie gevoerd en worden de bevindingen in een breder perspectief geplaatst. We geven aanbevelingen voor het verbeteren van de zorg en

voor het verrichten van toekomstig wetenschappelijk onderzoek. Het hoofdstuk eindigt met enkele conclusies.

CHAPTER 10

VALORISATION



INTRODUCTION

Society increasingly demands accountability for work performed, especially when public money is spent. This applies not only to business and government agencies, but also to scientific research.

Valorisation is ‘the process of creating value from knowledge, by making this knowledge available and suitable for economic and social exploitation and to translate this knowledge into products, services, processes and new business’. Therefore research results should be brought to attention of potential users and must be translated into social, economic and/or financial value.^{1,2}

ECONOMIC AND SOCIAL RELEVANCE OF RESULTS OF THIS THESIS

In this thesis we gave some suggestions for improvement of care during the hospitalization of Parkinson’s disease (PD) patients, e.g. self-administration of PD medication, proactive multidisciplinary approach, education of health care professionals, and prevention of infections and delirium (Chapter 3,4,5,6,7). These recommendations might eventually result in both economic and social valorisation.

Economic valorisation

In the Netherlands in 2011 the total number of patients with Parkinsonism was estimated 29,000. In the next decades the median age of the population will rise and as a result the number of PD patients will probably increase.^{3,4}

Patients with PD use a lot of healthcare facilities and as such related costs for PD and other forms of Parkinsonism are high. In the Netherlands in 2011 this was estimated at 267 million Euro per year.⁵⁻⁷ Hospital admissions account for 8.5% of these costs.⁷ We showed in this thesis that hospital stay is longer due to iatrogenic deterioration of PD symptoms. Strict adherence to our recommendations will most likely result in a decrease of length of hospital stay with concomitant decrease of costs. Although we didn’t do a proper cost-effectiveness study, which would be preferred, we can roughly estimate the unnecessary direct hospitalization costs concerning admissions with PD medication errors. Chapter 4 shows that medication errors occurred in 39% of admissions, which resulted, on average, in a longer hospitalization of 1.7 days compared to admissions without PD medication errors. PD hospitalization costs are estimated at 23 million Euro per year, spread over 1492 hospitalizations with an average duration of 12.6 days.⁷ If we extrapolate our findings to the Dutch situation it means that in 576 hospitalizations (i.e. 39% of total admission number) per year PD medication errors occur resulting in 979 extra hospitalization days (i.e. 576 x 1.7 days) per year. On average the cost of an admitted PD patient in The Netherlands health care system is 1,207 Euro

per day. This results, for the Netherlands only, in 1.18 million Euro per year of extra direct hospitalization costs because of PD medication errors, which is preventable and therefore unnecessary spent public money.

Improvement of care during hospitalization by implementing the recommendations of this thesis will result in reducing needless spending of both private and public money, which therefore becomes available for other (community related) purposes.

Social valorisation

PD has a high impact on quality of life of PD patients.⁸⁻¹⁰ Moreover, the patient is not the only one affected by the disease. Because of the disease, with both motor and non-motor symptoms, the patient needs a lot of attention by partner, children, and/or other caregivers, certainly in the more advanced stages of the disease. Now that the government has come up with the 'participation society' the pressure on the caregivers will only increase. A lot of these 'voluntary' caregivers have busy lives (own household, jobs), even without this extra care they (have to) provide. Although hospitalization of PD patients for some caregivers might be a temporarily relief, deterioration of PD symptoms will result in additional work after discharge from hospital.

This thesis shows that improvement of care during the hospitalization of PD patients will not only result in better health conditions of the PD patient but will also cause less distress and higher satisfaction for the caregiver.

PRODUCTS AND PROCESSES

To accomplish the recommendations, new developments will be valuable to implement. This could include an electronic notification that warns the hospital's Parkinson's team when a vulnerable PD patient is admitted. Another point of focus could be PD medication errors, for example by introducing a warning system that informs a nurse that the patient needs his or her medication. One option is a nurse's mobile phone notification on specific moments linked to the electronic medication systems (which may be coupled to the home pharmacy to provide an accurate home medication schedule). Another option, although maybe less effective but easier to introduce, could be the distribution of cards with (warning) instructions that the patient or caregiver can leave in the patient's room in case of hospitalization. Our data support the introduction of new (technological) products to improve hospital care to lead to both social and economic benefit.

TARGET GROUPS THAT CAN BENEFIT

PD patients are a vulnerable patient group for adverse events during hospitalization. One of the causes of these adverse events is due to difficult medication schemes. There are however more older patient groups with complex medication regimes that are at increased risk for complications during hospitalization. Examples are patients with dementia, cancer, and multimorbidity in general.¹¹

Other specialties and its patient population could benefit from the recommendations in this thesis to improve care, since most of these are generalizable. Next to this, the methods we used in this thesis to analyze a specific vulnerable patient group could be interesting for other patient groups as well. This could result in other specific recommendations to improve care for these patients.

CONCLUSION

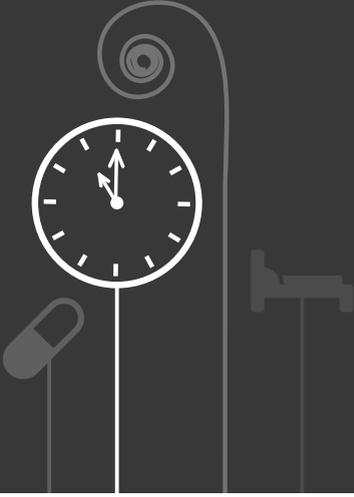
Valorisation of our study results are related to reduction of direct health care costs by strict adherence to our recommendations, which are easy to implement and to the development of new IT products based on our findings and recommendations that might be offered to the clinician to further improve care for PD patients. As such, our study and recommendations could lead to both economic and social valorisation.

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CHAPTER 11

ADDITIONAL FILES



ADDITIONAL FILE 1- INTRODUCTION LETTER QUESTIONNAIRE RETROSPECTIVE STUDY

Dear Sir/Madam,

You are being treated for Parkinson's disease in our hospital and/or you use drugs that are prescribed for this disease.

Many patients with Parkinson's disease have told us that they have deteriorated after a hospital stay. With this survey we would like to know your experience in this. With this information we strive to improve the quality of our patient care.

Therefore we would very much appreciate your cooperation to complete the attached questionnaire.

Confidential data processing

Personal information is strictly confidential and processed completely anonymously. Nobody will be able to determine on the basis of your answers who gave these answers.

Voluntary participation

Participation to this research is completely voluntary. You may refuse to participate without given a reason. Of course this will not influence your further treatment.

Questionnaire

You will notice that the questions resemble the questions normally asked by your treating doctor. We would *prefer* that you answer the questionnaire yourself (the patient), together with, if applicable, your partner or caregiver.

When answering the questions in case you are not the patient, all questions do relate to the patient.

Could you please return the questionnaire within two weeks. There is an envelope attached, there is no stamp required. You can also hand it over at the outpatient clinic.

If you have any questions or remarks concerning this survey please contact us: telephone number.

We try to maintain our address file as accurately as possible. Obviously, this questionnaire might have been delivered to you by mistake. It is also possible that this survey is sent to you on a very inappropriate moment for you or your family. If so, we apologize.

Thank you for your cooperation.

ADDITIONAL FILE 2 - QUESTIONNAIRE RETROSPECTIVE STUDY

A. General information

1. Who answers this questionnaire?

- Patient
- Patient with the help of partner or caregiver
- Partner and/or caregiver
- Other, namely(please mention the relationship with the patient)

2. What is your date of birth? (of the patient):

.....-.....-..... (day-month-year)

3. What is your gender?

- Male
- Female

4. What is your civil status?

- Living on your own
- Living together with partner, not married
- Living together with somebody else than partner, namely
- Married
- Widower/Widow
- Divorced
- Other, namely

5. What is your nationality?

- Dutch
- Belgium
- German
- Turkish
- Moroccan
- Other, namely

B. Care related questions

6. Have you been admitted to a hospital in the previous year?

No (go to question 18)

Yes, namely:

- Please mention all admissions both for neurology and other specialties, also if there were multiple admissions per specialty.

- Please mention for every admission if you did have surgery or not (cross out what is not applicable at 'Yes / No')

- Please mention all complications, if any, even if there were more than one per admission. Please mention if this complication was before and/or after a possible surgery (cross out what is not applicable at 'Before / after/ before and after').

(*Examples of complications:* Confusion, hallucinations, pneumonia, urinary tract infection, wound infections, thrombosis, falls, worsening of motor function, mood disorders, pulmonary embolism, memory impairment etc.)

Example 1 ..Internal medicine ...pneumonia... Yes/No no complication Before/after/before and after

2 ..Surgery... ..hipfracture... Yes / No ...thrombosis... Before/after/before and after

.....confusion... Before/after/before and after

Admission number	Specialty	illness/complaint	Surgery	Complication(s)	Before and/or after a possible surgery
1	Yes / No	Before/after/before and after
				Before/after/before and after
				Before/after/before and after
2	Yes / No	Before/after/before and after
				Before/after/before and after
				Before/after/before and after
3	Yes / No	Before/after/before and after
				Before/after/before and after
				Before/after/before and after
4	Yes / No	Before/after/before and after
				Before/after/before and after
				Before/after/before and after

- 5 Yes / No Before/after/before and after
 Before/after/before and after
 Before/after/before and after

The following questions can refer to an 'admission number', you can find it at question 6.

7. Was Parkinson's disease medication distributed according to the same schedule as you take your medication at home? (more than one answer possible)

- Not applicable, no admission
- Yes
- No, the time of medication distribution was not the same at admission number(s) (see question 6)
- No, the kind of Parkinson's disease medication did not match at admission number(s).....(see question 6)
- Don't know
- Other answer, namely

8. Was there during one of the admissions an interruption of Parkinson's disease medication? (more than one answer possible)

- Not applicable, no admission
- No
- Yes, during a surgery, namely at admission number(s)(see question 6)
- Yes, this was on purpose namely because ofat admission number(s).....(see question 6)
- Yes, this was not on purpose, namely at admission number(s)(see question 6)
- Don't know
- Other answer, namely

9. Did you have to point out to the personnel that there was a problem with the distribution of Parkinson's disease medication? (more than one answer possible)

- Not applicable, no admission
- No
- Yes, point out incorrect distribution time, namely at admission number(s).....(see question 6)
- Yes, point out incorrect Parkinson's disease medication, namely at admission number(s)(see question 6)
- Yes, point out that Parkinson's disease medication was forgotten, namely at admission number(s)(see question 6)
- Don't know
- Other answer, namely

10. Did you have to point out to the personnel that there was a problem with the distribution of Parkinson's disease medication after a possible surgery? (more than one answer possible)

- Not applicable, no surgery
- No, I did have surgery but there was no problem with the medication distribution after the surgery at admission number(s)(see question 6)
- Yes, point out incorrect Parkinson's disease medication, namely at admission number(s)(see question 6)
- Yes, point out that Parkinson's disease medication was forgotten, namely at admission number(s)(see question 6)
- Yes, point out that there was incorrect Parkinson's disease medication, namely at admission number(s)(see question 6)
- Don't know
- Other answer, namely

11. Was there a deterioration of Parkinson's disease (i.e. decline in motor function) during the admission? (more than one answer possible)

- Not applicable, no admission
- No, no deterioration (go to question 14)
- Yes, namely(please point out what aspect deteriorated) at admission number(s)(see question 6)
- Don't know
- Other answer, namely

12. Did this deterioration start after a possible surgery? (more than one answer possible)

- Not applicable, no surgery
- Not applicable, no deterioration
- No, deterioration started already before surgery, namely at admission number(s) (see question 6)
- Yes, deterioration started after surgery, namely at admission number(s)(see question 6)
- Don't know
- Other answer, namely

13. Did this deterioration start after interruption of Parkinson's disease medication?

- Not applicable, no admission
- Not applicable, no deterioration
- No
- Yes, namely at admission number(s)(see question 6)

- Don't know
- Other answer, namely

14. Was there a deterioration of Parkinson's disease after the admission?

- Not applicable, no admission
- No, no deterioration
- Yes, namely(please point out what aspect deteriorated) at admission number(s)(see question 6)
- Don't know
- Other answer, namely

15. How long did the deterioration of Parkinson's disease last? (more than one answer possible)

- Not applicable, no admission
- No deterioration during or after the admission at admission number(s)(see question 6)
- Deterioration lasted for: (if deterioration during or after more than one admission please mention the duration of all of them)
 -days, namely at admission number(s)(see question 6)
 -weeks
 -months
 -days, namely at admission number(s)(see question 6)
 -weeks
 -months
 -days, namely at admission number(s)(see question 6)
 -weeks
 -months
- No full recovery from deterioration, namely at admission number(s)(see question 6)
- Don't know

16. Was there contact with a Parkinson's disease nurse specialist or another allied healthcare facility during the admission? (for example occupational therapist, speech therapist, etc.)

- Not applicable, no admission
- No
- Don't know
- Yes, namely :
 - Parkinson's disease nurse specialist at admission number(s) (see question 6)
 - Physical therapy at admission number(s)(see question 6)

- Occupational therapy at admission number(s)(see question 6)
- Speech therapy at admission number(s)(see question 6)
- Psychology at admission number(s)(see question 6)
- Social worker at admission number(s)(see question 6)
- Another allied healthcare facility, namely:

<i>Allied healthcare facility</i>	admission number(s): see question 6
.....
.....

17. Do you use more frequently allied healthcare facilities after the admission compared to before?

- Not applicable, no admission
- Don't know
- No
- Yes, namely :
 - Parkinson's disease nurse specialist at admission number(s)
(see question 6)
 - Physical therapy at admission number(s)(see question 6)
 - Occupational therapy at admission number(s)(see question 6)
 - Speech therapy at admission number(s)(see question 6)
 - Psychology at admission number(s)(see question 6)
 - Social worker at admission number(s)(see question 6)
 - Another allied healthcare facility, namely:

<i>Allied healthcare facility</i>	admission number(s): see question 6
.....
.....

18. Where do you live now?:

- Independent house
- Assisted living
- Elderly home
- Nursing home
- Other answer, namely

**19. If you use medication, do you take the medication as prescribed by the doctor?
(more than one answer possible)**

- Yes, the correct medication at the correct times
- No, I don't take the medication at all
- No, I sometimes forget medication
- No, I often forget medication

- No, I don't take the medication at the prescribed times because
- No, I often take extra medication because of
- No, I often don't take medication because of side effects
- No, I often don't take medication because of the costs
- No, I often don't take medication because I have too many tablets
- Other answer, namely

C. Disease relates questions

20. Do you have (had) tremors? (more than one answer possible)

- No
- Yes, the head
- Yes, the arms/hands
- Yes, the legs/feet
- Other answer, namely

21. Do you have (had) stiffness/rigidity? (more than one answer possible)

- No
- Yes, the arms
- Yes, the legs
- Other answer, namely

22. Do you have (had) bradykinesia or did you become slower because of Parkinson's disease?

- No
- Yes

23. Do you have (had) postural instability?

- No
- Yes, but I never fall
- Yes, I fall sometimes
- Yes, I fall often
- Yes, I can not walk anymore
- Other answer, namely

24. If you fall, how often do you fall on average per month?

..... times on average per month

25. In what year did the symptoms (as described in question 2□ to 24) of Parkinson's disease begin?

- In the year :
- Not applicable
- Don't know

26. Do you currently have one or more of the following symptoms? (more than one answer possible)

- Problems with turning over in bed
- Reduced smell
- Problems with writing
- Problems with using cutlery
- Joint pain
- Back pain
- Cramps
- Pain, namely
- Changed sexual behaviour, namely
- Psychosis/hallucinations
- Dyskinesia
- On-off moments
- Depressed mood
- Anxiety and/or panic attacks
- Light-headedness when standing quickly
- Swallow problems
- Choking
- Problems with urination
- Problems with defecation
- Memory problems
- Behaviour problems
- Sensation of tingling (paresthesia)
- Sleep disorders
- Problems with breathing, namely
- Other answer, namely

27. Which of the following answers fits you the most? (just one answer possible)

- No signs of the disease
- Unilateral symptoms only, no impairment of balance
- Bilateral symptoms, no impairment of balance
- Mild to moderate disease symptoms, balance impairment, physically independent

- Severe disability, but still able to walk or stand unassisted
- Needing a wheelchair or bedridden unless assisted

28. Do you currently take medication?

- Yes
- No (go to question 30)

29. What medication do you currently take? (all drugs for all diseases)

Please also mention any side effects.

Optionally, a copy of your medication prescriptions can be added.

(Example: sinemet 125mg 3 times per day 2 tablets Drowsiness)

Name of drugs:	Dose	How many times a day how many tablets	Side effect
----------------	------	--	-------------

- | | | | |
|----|-------|-------|-------|
| 1 | | | |
| 2 | | | |
| 3 | | | |
| 4 | | | |
| 5 | | | |
| 6 | | | |
| 7 | | | |
| 8 | | | |
| 9 | | | |
| 10 | | | |
| 11 | | | |

30. Do you have any questions or remarks concerning this survey?

.....

.....

.....

END OF QUESTIONNAIRE

Could you please verify that you have answered all the questions completely?

ADDITIONAL FILE 3 - QUESTIONNAIRE PROSPECTIVE STUDY

Timepoint 1

A. General information

1. Patient identification number:

2. Investigator:

3. Date of measurement ...-...-... (day-month-year)

4. Day of inclusion:

Day 1

Day ...

Because of:

Patient related issues, namely ...

Logistic reasons, namely ...

Other reasons, namely

5. What is your age?

..... years

6. What is your gender?

Male

Female

7. What is your civil status?

Living on your own

Living together with partner, not married

Living together with somebody else than partner, namely

Married

Widower/Widow

Divorced

Other, namely

8. Where do you live?

- In a house, independent
- Assisted living
- Home for the elderly
- Nursing home
- Other, namely

B. Disease related questions

9. How many years ago did the Parkinson disease related symptoms start?

- years
- Unknown

10. Do you often fall at home?

- No, never.
- Yes, approximately times a month

11. Do you currently have one or more of the following symptoms? (more than one answer possible)

- Problems with turning in bed
- Reduced smell
- Problems with writing
- Problems with using cutlery
- Joint pain
- Back pain
- Cramps
- Pain, namely
- Changed sexual behaviour, namely
- Psychosis/hallucinations
- Dyskinesia
- On-off moments
- Depressed mood
- Anxiety and/or panic attacks
- Light-headedness when standing quickly
- Swallow problems
- Choking
- Problems with urination
- Problems with defecation
- Memory problems
- Behavior problems

- Sensation of tingling (paresthesia)
- Sleep disorders
- Problems with breathing, namely
- Other answer, namely

12. Do you have, besides Parkinson’s disease, other medical conditions? (more than one answer possible).

- No
- Yes, hypertension
- Yes, diabetes
- Yes, heart problems namely
- Yes, persistent neurologic deficit after a stroke, namely
- Yes, epilepsy
- Yes, kidney disease, namely
- Yes, liver disease, namely
- Yes, artrosis of the joints
- Yes, rheumatoid arthritis
- Yes, osteoporosis
- Yes, cataract
- Yes, enlarged prostate
- Yes, skin disease namely
- Yes, cancer, namely
- Yes, other, namely

13. Are you currently using any medication?

- Yes
- No

14. If you are using medication, which one? (every medication for all medical conditions).

Medication name:	Dose	Times a day
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		

- 10.
- 11.
- 12.
- 13.
- 14.
- 15.

15. At home, do you use your Parkinson medication accordingly to the schedule as prescribed by your doctor?

- Not applicable, not using Parkinson medication
- No, different timing because
- No, not taking some pills because
- Yes
- Other, namely

C. Care related questions

16. What is the admission reason (diagnose and complaints)?

17. For what specialty are you currently admitted?

18. Is it a planned/elective admission?

- No
- Yes
- Other, namely

19. Is it an emergency admission?

- No
- Yes
- Other, namely

20. Are you admitted through the emergency department?

- No
- Yes
- Other, namely

21. Did you have surgery?

- No

Yes, namely

1. Urgency/planned
2. Urgency/planned
3. Urgency/planned
4. Urgency/planned

(please mention all surgeries, and what sort of surgery you had)

Other, namely

22. Were there any complications during your stay in the hospital?

Please note all complications, and point out if they happened before or after surgery (if applicable). Examples of complications (walkthrough with patient):

Confusion, delirium, hallucinations, decubitus ulcer, wound infections, pneumonia, upper airway infection, cystitis, other infections, bladder problems, constipation, cardiovascular events, TIA, stroke, deep venous thrombosis, fall, fractures, gastrointestinal problems, pain, deterioration of motor function, increased rigidity, mood problems, pulmonary embolism, memory problems, etc.

No

Yes

Complication(s): Before and/or after surgery

- a. Before/ After/ Before and after/During/ Not applicable
- b. Before/ After/ Before and after/During/ Not applicable
- c. Before/ After/ Before and after/During/ Not applicable
- d. Before/ After/ Before and after/During/ Not applicable
- e. Before/ After/ Before and after/During/ Not applicable

23. Was there during this admission an episode of confusion / delirium?

No

Yes.

If answered yes, please point out the confusion / delirium was yet present before hospitalization:

No, not present before hospitalization

Yes, present before hospitalization

Don't know

24. Are there any other specialists consulted during the admission?

No

Yes, namely

1. Specialty:..... Reason:
2. Specialty:..... Reason:
3. Specialty:..... Reason:

- 4. Specialty:..... Reason:
- 5. Specialty:..... Reason:
- 6. Specialty:..... Reason:

Other, namely.....

25. Is the patient currently admitted to the intensive care unit (ICU)?

No

Yes, Specialty:
 Reason:
 Length (days):
 Course:

Consulted specialists:

- 1. Specialty:..... Reason:
- 2. Specialty:..... Reason:
- 3. Specialty:..... Reason:
- 4. Specialty:..... Reason:
- 5. Specialty:..... Reason:
- 6. Specialty:..... Reason:

Complication(s):

- a. Before/ After/ Before and after/During/ Not applicable
- b. Before/ After/ Before and after/During/ Not applicable
- c. Before/ After/ Before and after/During/ Not applicable
- d. Before/ After/ Before and after/During/ Not applicable

26. Is the patient currently admitted to the medium care unit (MCU)?

No

Yes, Specialty:
 Reason:
 Length (days):
 Course:

Consulted specialists:

- 1. Specialty:..... Reason:
- 2. Specialty:..... Reason:
- 3. Specialty:..... Reason:
- 4. Specialty:..... Reason:
- 5. Specialty:..... Reason:
- 6. Specialty:..... Reason:

Complication(s):

- a. Before/ After/ Before and after/During/ Not applicable
- b. Before/ After/ Before and after/During/ Not applicable

- c. Before/ After/ Before and after/During/ Not applicable
- d. Before/ After/ Before and after/During/ Not applicable

27. Did you fall during the hospital stay?

- No
- Yes, times

If you did, please point out if this was before of after surgery (if applicable):

- 1. Before/ After/ Before and after/During/ Not applicable
- 2. Before/ After/ Before and after/During/ Not applicable
- 3. Before/ After/ Before and after/During/ Not applicable
- 4. Before/ After/ Before and after/During/ Not applicable

- Don't know
- Other, namely

28. Was Parkinson's disease medication distributed according to the same schedule as you take your medication at home? (more than one answer possible)

- Not applicable, no Parkinson's disease medication
- Yes
- No, the time of medication distribution was not the same
- No, the kind of Parkinson's disease medication did not match
- Don't know
- Other answer, namely

29. Was there during one of the admissions an interruption of Parkinson's disease medication? (more than one answer possible)

- Not applicable, no Parkinson's disease medication
- No
- Yes, during surgery
 - Length of interruption: hours/ days
 - If more than one surgery, please write down all interruptions.
- Yes, this was on purpose because of
- Yes, this was not on purpose
- Don't know
- Other answer, namely

30. Did you have to point out to the personnel that there was a problem with the distribution of Parkinson's disease medication? (more than one answer possible)

- Not applicable, no Parkinson's disease medication
- No
- Yes, point out incorrect distribution time

- Yes, point out incorrect Parkinson's disease medication
- Yes, point out that Parkinson's disease medication was forgotten
- Don't know
- Other answer, namely

31. Did you have to point out to the personnel that there was a problem with the distribution of Parkinson's disease medication after a possible surgery? (more than one answer possible)

- Not applicable, no Parkinson's disease medication
- Not applicable, no surgery
- No, I did have surgery but there was no problem with the medication distribution after the surgery.
- Yes, point out incorrect Parkinson's disease medication
- Yes, point out that Parkinson's disease medication was forgotten
- Yes, point out that there was incorrect Parkinson's disease medication
- Don't know
- Other answer, namely

32. Was there deterioration of Parkinson's disease (i.e. decline in motor function) during the admission? (more than one answer possible)

- No, no deterioration
- Yes, namely(please point out what aspect deteriorated)
- Don't know
- Other answer, namely

33. Did this deterioration start after a possible surgery? (more than one answer possible)

- Not applicable, no surgery
- Not applicable, no deterioration
- No, deterioration started already before surgery
- Yes, deterioration started after surgery
- Don't know
- Other answer, namely

34. Did this deterioration start after interruption of Parkinson's disease medication?

- Not applicable, no Parkinson's disease medication
- Not applicable, no deterioration
- Not applicable, no surgery
- No
- Yes
- Don't know

Other answer, namely

35. Was there contact with a Parkinson's disease nurse specialist or another allied healthcare facility during the admission? (for example occupational therapist, speech therapist, etc.)

No

Don't know

Yes, namely :

Parkinson's disease nurse specialist

Physical therapy

Occupational therapy

Speech therapy

Psychology

Social worker

Another allied healthcare facility, namely:

Allied healthcare facility

.....

.....

36. Did the investigator contact the nurses or/and doctors about any health related problems concerning the patient?

No

Yes, contact with: nurse / doctor / consultant/ other

concern and advise:

therapeutic consequence:

37. Comments

.....
.....
.....
.....

Timepoint 2

A. General information

1. Patient identification number:

2. Investigator:

3. Day of examination:

4. If it's not the last or next-to-last day of the admission please point out the reason:

Patient related issues, namely.....

Logistic reasons, namely.....

Other, namely.....

B. Disease related questions

5. If you are using medication, which one? (every medication for all medical conditions)

Medication name:	Dose	Times a day
------------------	------	-------------

1.

2.

3.

4.

5.

6.

7.

8.

C. Care related questions

6. Is the diagnosis at admission identical to the diagnosis at discharge?

Yes, the diagnosis didn't change and there were no additional diagnoses.

Yes, the diagnosis didn't change but there were additional diagnoses.

No

Other, namely

7. What is the definitive diagnosis at discharge? (please note all diagnoses)

1.

2.

3.

4.

Other, namely

8. For what specialty are you admitted? (if there are more than one please note all specialties).

1.

2.

3.

4.

9. Are there any other specialists consulted during the admission?

No

Yes, namely

1. Specialty:..... Reason:

2. Specialty:..... Reason:

3. Specialty:..... Reason:

4. Specialty:..... Reason:

5. Specialty:..... Reason:

6. Specialty:..... Reason:

Other, namely.....

10. Did you had surgery?

No

Yes, namely (please mention if the surgery was planned/elective or urgency)

1. Urgency/planned

2. Urgency/planned

3. Urgency/planned

4. Urgency/planned

(please mention all surgery, and what sort of surgery you had)

Other, namely

11. Were there any complications during your stay in the hospital?

Please note all complications, and point out if they happened before or after surgery (if applicable). Examples of complications (walkthrough with patient):

Confusion, delirium, hallucinations, decubitus, ulcer, wound infections, pneumonia, upper airway infection, cystitis, other infections, bladder problems, constipation, cardiovascular

events, TIA, stroke, deep venous thrombosis, fall, fractures, gastrointestinal problems, pain, deterioration of motor function, increased rigidity, mood problems, pulmonary embolism, memory problems, etc.

No

Yes

Complication(s): Before and/or after surgery

a. Before/ After/ Before and after/During/ Not applicable

b. Before/ After/ Before and after/During/ Not applicable

c. Before/ After/ Before and after/During/ Not applicable

d. Before/ After/ Before and after/During/ Not applicable

e. Before/ After/ Before and after/During/ Not applicable

f. Before/ After/ Before and after/During/ Not applicable

12. Was there during this admission an episode of confusion / delirium?

No

Yes.

If answered yes, please point out the confusion / delirium was yet present before hospitalization:

No, not present before hospitalization

Yes, present before hospitalization

Don't know

13. Did you fall during the hospital stay?

No

Yes, times

If you did, please point out if this was before of after surgery (if applicable):

1. Before/ After/ Before and after/During/ Not applicable

2. Before/ After/ Before and after/During/ Not applicable

3. Before/ After/ Before and after/During/ Not applicable

4. Before/ After/ Before and after/During/ Not applicable

Don't know

Other, namely

14. Was Parkinson's disease medication distributed according to the same schedule as you take your medication at home? (more than one answer possible)

Not applicable, no Parkinson's disease medication

Yes

No, the time of medication distribution was not the same

No, the kind of Parkinson's disease medication did not match

Don't know

Other answer, namely

15. Was there during one of the admissions an interruption of Parkinson's disease medication? (more than one answer possible)

Not applicable, no Parkinson's disease medication

No

Yes, during surgery

Length of interruption: hours/ days

If more than one surgery, please write down all interruptions.

Yes, this was on purpose because of

Yes, this was not on purpose

Don't know

Other answer, namely

16. Did you have to point out to the personnel that there was a problem with the distribution of Parkinson's disease medication? (more than one answer possible)

Not applicable, no Parkinson's disease medication

No

Yes, point out incorrect distribution time

Yes, point out incorrect Parkinson's disease medication

Yes, point out that Parkinson's disease medication was forgotten

Don't know

Other answer, namely

17. Did you have to point out to the personnel that there was a problem with the distribution of Parkinson's disease medication after a possible surgery? (more than one answer possible)

Not applicable, no Parkinson's disease medication

Not applicable, no surgery

No, I did have surgery but there was no problem with the medication distribution after the surgery.

Yes, point out incorrect Parkinson's disease medication

Yes, point out that Parkinson's disease medication was forgotten

Yes, point out that there was incorrect Parkinson's disease medication

Don't know

Other answer, namely

18. Was there deterioration of Parkinson's disease (i.e. decline in motor function) during the admission? (more than one answer possible)

No, no deterioration

Yes, namely(please point out what aspect deteriorated)

- Don't know
- Other answer, namely

19. Did this deterioration start after a possible surgery? (more than one answer possible)

- Not applicable, no surgery
- Not applicable, no deterioration
- No, deterioration started already before surgery
- Yes, deterioration started after surgery
- Don't know
- Other answer, namely

20. Did this deterioration start after interruption of Parkinson's disease medication?

- Not applicable, no Parkinson's disease medication
- Not applicable, no deterioration
- Not applicable, no surgery
- No
- Yes
- Don't know
- Other answer, namely

21. Did this deterioration start after transfer to other department? (more than one answer possible)

- Not applicable, no transfer
- Not applicable, no deterioration
- No, deterioration started already before transfer
- Yes, deterioration started after transfer
- Don't know
- Other answer, namely

22. Was there contact with a Parkinson's disease nurse specialist or another allied healthcare facility during the admission? (for example occupational therapist, speech therapist, etc.)

- No
- Don't know
- Yes, namely :
 - Parkinson's disease nurse specialist
 - Physical therapy
 - Occupational therapy
 - Speech therapy
 - Psychology

- Social worker
- Another allied healthcare facility, namely:
Allied healthcare facility
.....
.....

23. Number of days in the hospital:

..... Days.

24. Do you return to your original home after discharge?

- Yes
- No, change of housing situation:
New housing: Permanent/ Temporary
- Other, namely

25. Did the investigator contact the nurses or/and doctors about any health related problems concerning the patient?

- No
- Yes, contact with: nurse / doctor / consultant/ other
concern and advise:
therapeutic consequence:

28. Comments

.....
.....
.....
.....

ADDITIONAL FILE 4 - QUESTIONNAIRE HOSPITALS

Questionnaire number:

Name hospital:

1. What is your profession?

- Non-academic neurologist
- Academic neurologist
- Non-academic neurologist with special expertise on movement disorders
- Academic neurologist with special expertise on movement disorders
- Parkinson's disease nurse specialist
- Other, namely

2. In what type of hospital do you work?

- Non-academic
- Academic
- Other, namely

3. How many neurologists work in your hospital?

.....

4. How many people live in the catchment area of your hospital?

- <50.000
- 50.000-100.000
- 100.000-150.000
- 150.000-200.000
- 200.000-250.000
- More, namely

5. How many patients do you have in your hospital with the following diagnosis?

- Parkinson's disease:
- Parkinsonism:

6. Is neurology involved during the hospitalization of patients with Parkinson's disease for another speciality than neurology?

- No
- Yes, always
- Yes, on specific request of the treating specialist

- Yes, on specific request of the hospitalized patient
- Other, namely

7. In your hospital, is there a system to trace admitted Parkinson's disease patients during the hospitalization for another specialty than neurology?

- No
- Yes, the patient is asked to inform the treating specialist
- Yes, through
- Other, namely

8. In your hospital, is there a Parkinson's disease nurse specialist?

- No (go to question 11)
- Yes

9. Is the Parkinson's disease nurse specialist involved during the hospitalization of Parkinson's disease patients for another specialty than neurology?

- No
- Yes
- Other, namely

10. Are there, because of the Parkinson's disease nurse specialist, less admissions of Parkinson's disease patients?

A for Neurology?

- Yes
- Yes, I think
- Yes, I know
- Other, namely

B for another specialty?

- Yes
- Yes, I think
- Yes, I know
- Other, namely

11. Is neurology involved perioperatively for a patient with Parkinson's disease that is going to have surgery?

- No, never (go to question 12)
- Yes:

A

- Yes, always
- Yes, on specific request of the treating specialist
- Other, namely

B

- Yes, during all kind of surgeries
- Yes, during special types of surgeries
namely

C

- Yes, before surgery
- Yes, after surgery
- Yes, during surgery
- Yes, before, during and after surgery

D

- Yes, only local anesthesia
- Yes, only short general anesthesia
- Yes, only long general anesthesia
- Yes, both short and long anesthesia
- Yes, both local and general anesthesia

E

- Yes, if the threatening specialist expects neurological complications
- Yes, only if neurological complications have occurred
- Yes, also if there are no neurological complications expected
- Other, namely

F

- Yes, only planned surgery
- Yes, only emergency surgery
- Yes, both planned and emergency surgery

12. Is there in your hospital a protocol available with regard to patients with Parkinson's disease having surgery?

- No (go to question 13)
- Yes

A

If yes, it concerns

- Advice before surgery
- Advice during surgery
- Advice after surgery
- Advice before, during and after surgery

B

If yes, is it advice with regard to medication?

- Yes, only medication advice
- Yes, but also other advice namely
- No, other advice namely

C

If yes, could you send it to us?

- Yes
- No

13. Do you use parenteral dopaminergic medication perioperatively in your hospital for Parkinson's disease patients that use PD medication?

- No, never
- Yes, always
- Yes, only if indicated namely

If yes it concerns

14. Is there a medication list available in your hospital that shows interaction between different types of medication with PD medication?

- No
- Yes, available at neurology
- Yes, available at neurology and on specific request for other specialties
- Yes, available for all specialties
- Yes, namely

15. Could you make an estimation how often per year neurology is involved perioperatively for complications with regard to PD patients?

A

- No, neurology is never involved
- No, neurology is involved but I don't now how often
- Yes, estimated times per year

Yes, this is recorded namely times per year

B Which complications do you see? (more answers possible)

Number

- Pulmonological problems, especially
- Cardial problems, especially
- Gastrointestinal problems, especially
- Autonomic nervous system problems, especially
- Motor problems, especially
- Cognitive problems, especially
- Delirium
- Other, namely

Could you please indicate which complications you see the most by writing down a number from 1 to 8 behind the answers of 15B: most frequent one is number 1 and less frequent is number 8.

16. Could you make an estimation how often per year neurology is involved postoperatively for complications with regard to PD patients?

A

- No, neurology is never involved
- No, neurology is involved but I don't know how often
- Yes, estimated times per year
- Yes, this is recorded namely times per year

B Which complications do you see? (more answers possible)

Number

- Pulmonological problems, especially
- Cardial problems, especially
- Gastrointestinal problems, especially
- Autonomic nervous system problems, especially
- Motor problems, especially
- Cognitive problems, especially
- Delirium
- Other, namely

Could you please indicate which complications you see the most by writing down a number from 1 to 8 behind the answers of 16B: most frequent one is number 1 and less frequent is number 8.

Remarks:

.....

.....

.....

.....

.....

.....

LIST OF PUBLICATIONS

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DANKWOORD

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CURRICULUM VITAE

Oliver Henricus Hubertus Gerlach was born on the 18th of Februari 1978 in Usingen, Germany. He lived his first 4 years in Wehrheim, Germany, and then moved to Weert, The Netherlands. He graduated for secondary school, Gymnasium, at the Bisschoppelijk College in Weert in 1996. From 1996 untill 2000, he studied medicine at the Catholic University Leuven, Belgium. In 2000, he continued his medical training at the Maastricht University. He received his doctoral diploma in medicine with first class honours and received his medical doctor degree in 2005. The same year he started his working career as a clinical resident in Neurology at the Maaslandziekenhuis, Sittard-Geleen. In 2006, he started his training in Neurology at the Maastricht University Medical Centre+ and finished this May 2012. Since then he works as a neurologist at the Zuyderland Medical Centre.

In 2008 he started with his PhD at the department of Neurology of the Maastricht University Medical Centre+, investigating the problems Parkinson's disease patients encounter during hospitalization.

Oliver Henricus Hubertus Gerlach werd op 18 februari 1978 geboren in Usingen, Duitsland. Na 4 jaar in Wehrheim, Duitsland, gewoond te hebben verhuisde hij naar Weert, Nederland. In 1996 behaalde hij het eindexamen van het gymnasium aan het Bisschoppelijk College in Weert. Van 1996 tot 2000 studeerde hij geneeskunde aan de Katholieke Universiteit Leuven in België. Hij vervolgde zijn opleiding dat jaar aan de faculteit der geneeskunde van de Universiteit Maastricht. Hij behaalde zijn doctoraalexamen cum laude en nam in 2005 zijn arts diploma in ontvangst. Dat jaar begon hij te werken als arts-assistent op de afdeling neurologie van het Maaslandziekenhuis te Sittard-Geleen. In 2006 startte hij met de opleiding tot neuroloog aan het Maastricht Universitair Medisch Centrum+ en runde deze mei 2012 af. Sindsdien werkt hij als neuroloog in het Zuyderland Medisch Centrum. In 2008 begon hij aan de afdeling neurologie van het Maastricht Universitair Medisch Centrum+ aan zijn onderzoek naar problemen tijdens de ziekenhuisopnames van patiënten met de ziekte van Parkinson.

