

Parkinson's Disease Current Awareness Bulletin

August 2023

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1. Screening Tools for Sarcopenia in Mild to Moderate Parkinson's Disease: Assessing the Accuracy of SARC-F and Calf Circumference.

Authors: de Luna, J. R. G.;Lima, D. P.;Gomes, V. C.;de Almeida, S. B.;Monteiro, P. A.;VianaJunior, A. B.;Marques da Silva, T. A.;Gradvohl, L. B.;Bruno, L. B.;Lindsay Silva Marques, M.;Cunha, L. C. V.;Feitosa, C. X.;BragaNeto, P.;RorizFilho, J. S. and MontenegroJunior, R. M.

Publication Date: 2023

Journal: Journal of Parkinson's Disease (pagination), pp. ate of Pubaton: 12 Ju 2023

Abstract: BACKGROUND: Parkinson's disease (PD) and sarcopenia share similar pathophysiological mechanisms. OBJECTIVE(S): Estimate the prevalence of sarcopenia in PD patients and describe clinical and demographic features associated with sarcopenia. METHOD(S): A cross-sectional study was carried out at a tertiary public hospital in Brazil. A modified HY scale of stage 1 to 3, being at least 40 years old and having the ability to stand and walk unassisted were required for eligibility. We evaluated physical performance and muscle mass using DEXA. RESULT(S): The study population comprised 124 patients, of which 53 (42.7%) were women. The mean age and mean disease duration were 65.8+/-10.5 and 10.1+/-5.8 years, respectively. The mean handgrip strength of 20.4+/-6.9 in woman and 34.6+/-8.4 kg in men. Moreover, 50.8% patients had positive SARC-F, 20% patients had probable sarcopenia, 9.6% confirmed sarcopenia, and 16.8% patients showed low muscle mass quantity measured by DEXA. Lower Levodopa Equivalent Dosage (LED) and calf circumference (CC) were independently associated with confirmed sarcopenia. LLED, higher MDS-UPDRS Part III, and lower MMSE scores were independently associated with probable sarcopenia. The CC demonstrated accuracy to identify PD patients with confirmed sarcopenia with a cut-off of RESULT(S): The study population comprised 124 patients, of which 53 (42.7%) were women. The mean age and mean disease duration were 65.8+/-10.5 and 10.1+/-5.8 years, respectively. The mean handgrip strength of 20.4+/-6.9 in woman and 34.6+/-8.4 kg in men. Moreover, 50.8% patients had positive SARC-F, 20% patients had probable sarcopenia, 9.6% confirmed sarcopenia, and 16.8% patients showed low muscle mass quantity measured by DEXA. Lower Levodopa Equivalent Dosage (LED) and calf circumference (CC) were independently associated with confirmed sarcopenia. LLED, higher MDS-UPDRS Part III, and lower MMSE scores were independently associated with probable sarcopenia. The CC demonstrated accuracy to identify PD patients with confirmed sarcopenia with a cut-off of RESULT(S): The study population comprised 124 patients, of which 53 (42.7%) were women. The mean age and mean disease duration were 65.8+/-10.5 and 10.1+/-5.8 years, respectively. The mean handgrip strength of 20.4+/-6.9 in woman and 34.6+/-8.4 kg in men. Moreover, 50.8% patients had positive SARC-F, 20% patients had probable sarcopenia, 9.6% confirmed sarcopenia, and 16.8% patients showed low muscle mass quantity measured by DEXA. Lower Levodopa Equivalent Dosage (LED) and calf circumference (CC) were independently associated with confirmed sarcopenia. LLED, higher MDS-UPDRS Part III, and lower MMSE scores were independently associated with probable sarcopenia. The CC demonstrated accuracy to identify PD patients with confirmed sarcopenia with a cut-off of CONCLUSION(S): We found low prevalence of confirmed sarcopenia among PD patients. We propose that healthcare providers introduce measuring CC, which is a quick and inexpensive method to assess for sarcopenia in PD patients

2. Characteristics and outcomes of elderly patients with Parkinson's disease hospitalized due to COVID-19-associated pneumonia.

Authors: Georgakopoulou, Vasiliki Epameinondas;Gkoufa, Aikaterini;Bougea, Anastasia;Basoulis, Dimitrios;Tsakanikas, Aristeidis;Makrodimitri, Sotiria;Karamanakos, Georgios;Spandidos, Demetrios A.;Angelopoulou, Efthalia and Sipsas, Nikolaos V.

Publication Date: 2023

Journal: Medicine International 3(4), pp. 34

Abstract: Patients with Parkinson's disease (PD) and coronavirus disease 2019 (COVID-19)-associated pneumonia present, according to the literature, high mortality rates due to the nature of the disease, advanced age, and underlying diseases. Most available studies, however, refer to the first waves of the pandemic. The aim of the present study was to investigate the clinical characteristics and outcomes of elderly patients (≥ 65 years old) with PD hospitalized with COVID-19-associated pneumonia during the period of prevalence of various severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants, as well as to determine possible prognostic factors for poor outcomes. During the period from February 15, 2021, to July 15, 2022, 1,144 elderly patients with COVID-19 pneumonia were hospitalized. Age, sex, Charlson comorbidity index, vaccination status against SARS-CoV-2, and admission laboratory parameters were recorded for all patients. A total of 36 (3.1%) patients with PD were hospitalized due to COVID-19-associated pneumonia (18 males, 50%). The mean age of the patients was 82.72 ± 8.18 years. In total, 8 patients (22.2%) were hospitalized during the period of alpha variant predominance, 3 patients (8.3%) during the period of delta variant predominance, and 25 patients (69.4%) during the omicron variant predominance period. Of note, 16 patients (44.4%) were vaccinated with at least two doses. In addition, 17 (47.2%) patients succumbed to the disease. Between the patients who survived and those who succumbed, a statistically significant difference was only found in the mean value of albumin (37.48 ± 6.02 vs. 31.97 ± 5.34 g/l, $P=0.019$). In particular, as shown by receiver operating characteristic curve analysis, albumin exhibited a satisfactory predictive ability for mortality (area under the curve, 0.780; $P=0.013$) with an albumin value

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3. Long-term effects of subthalamic nucleus deep brain stimulation on speech in Parkinson's disease.

Authors: Gessani, Annalisa;Cavallieri, Francesco;Fioravanti, Valentina;Campanini, Isabella;Merlo, Andrea;Di Rauso, Giulia;Damiano, Benedetta;Scaltriti, Sara;Bardi, Elisa;Corni, Maria Giulia;Antonelli, Francesca;Cavalleri, Francesca;Molinari, Maria Angela;Contardi, Sara;Menozi, Elisa;Fraternali, Alessandro;Versari, Annibale;Biagini, Giuseppe;Fraix, Valerie;Pinto, Serge, et al

Publication Date: Jul 15 ,2023

Journal: Scientific Reports 13(1), pp. 11462

Abstract: Bilateral subthalamic nucleus deep brain stimulation (STN-DBS) is an effective treatment in advanced Parkinson's Disease (PD). However, the effects of STN-DBS on speech are still debated, particularly in the long-term follow-up. The objective of this study was to evaluate the long-term effects of bilateral STN-DBS on speech in a cohort of advanced PD patients treated with bilateral STN-DBS. Each patient was assessed before surgery through a neurological evaluation and a perceptual-acoustic analysis of speech and re-assessed in the long-term in different stimulation and drug conditions. The primary outcome was the percentage change of speech intelligibility obtained by comparing the postoperative on-stimulation/off-medication condition with the preoperative off-medication condition. Twenty-five PD patients treated with bilateral STN-DBS with a 5-year follow-up were included. In the long-term, speech intelligibility stayed at the same level as preoperative values when compared with preoperative values. STN-DBS induced a significant acute improvement of speech intelligibility (p Copyright © 2023. The Author(s).

4. Risk and protective factors in Parkinson's disease: a simultaneous and prospective study with classical statistical and novel machine learning models.

Authors: Gialluisi, Alessandro;De Bartolo, Maria Ilenia;Costanzo, Simona;Belvisi, Daniele;Falciglia, Stefania;Ricci, Moreno;Di Castelnuovo, Augusto;Panzerà, Teresa;Donati, Maria Benedetta;Fabbrini, Giovanni;de Gaetano, Giovanni;Berardelli, Alfredo and Iacoviello, Licia

Publication Date: Sep ,2023

Journal: Journal of Neurology 270(9), pp. 4487-4497

Abstract: BACKGROUND: Several environmental/lifestyle factors have been individually investigated in previous Parkinson's disease (PD) studies with controversial results. No study has prospectively and simultaneously investigated potential risk/protective factors of PD using both classical statistical and novel machine learning analyses. The latter may reveal more complex associations and new factors that are undetected by merely linear models. To fill this gap, we simultaneously investigated potential risk/protective factors involved in PD in a large prospective population study using both approaches. METHODS: Participants in the Moli-sani study were enrolled between 2005 and 2010 and followed up until December 2018. Incident PD cases were identified by individual-level record linkage to regional hospital discharge forms, the Italian death registry, and the regional prescription register. Exposure to potential risk/protective factors was assessed at baseline. Multivariable Cox Proportional Hazards (PH) regression models and survival random forests (SRF) were built to identify the most influential factors. RESULTS: We identified 213 incident PD cases out of 23,901 subjects. Cox PH models revealed that age, sex, dysthyroidism and diabetes were associated with an increased risk of PD. Both hyper and hypothyroidism were independently associated with PD risk. SRF showed that age was the most influential factor in PD risk, followed by coffee intake, daily physical activity, and hypertension. CONCLUSION: This study sheds light on the role of dysthyroidism, diabetes and hypertension in PD onset, characterized to date by an uncertain relationship with PD, and also confirms the relevance of most factors (age, sex, coffee intake, daily physical activity) reportedly shown be associated with PD. Further methodological developments in SRF models will allow to untangle the nature of the potential non-linear relationships identified. Copyright © 2023. The Author(s), under exclusive licence to Springer-Verlag GmbH Germany.

5. Opicapone versus entacapone: Head-to-head retrospective data-based comparison of healthcare resource utilization in people with Parkinson's new to COMT inhibitor treatment.

Authors: HarrisonJones, G.;Marston, X. L.;Morgante, F.;Ray Chaudhuri, K.;CastillaFernandez, G. and Foggia, V. D.

Publication Date: 2023

Journal: European Journal of Neurology (pagination), pp. ate of Pubaton: 25 Ju 2023

Abstract: INTRODUCTION: Motor fluctuations are a significant driver of healthcare resource utilization (HCRU) in people with Parkinson's (PwP). A common management strategy is to include Catechol-O-methyl transferase (COMT) inhibition with either opicapone or entacapone in the levodopa regimen. However, to date, there has been a lack of head-to-head data comparing the two COMT inhibitors in real-world settings. METHOD(S): In this

retrospective cohort study, we assessed HCRU outcomes in PwP naive to COMT inhibition via UK electronic healthcare records (Clinical Practice Research Datalink and Hospital Episodes Statistics databases, June 2016 to December 2019). HCRU outcomes were assessed before (baseline) and after COMT inhibitor prescription at 0-6 months, 7-12 months, and 13-18 months. Opicapone treated PwP were algorithm-matched (1:4) to entacapone-treated PwP. RESULT(S): By 6-months, treatment with opicapone resulted in 18.5% fewer neurology outpatient visits compared to entacapone treatment; this effect was maintained until the last follow-up (18-months). In the opicapone group, the mean levodopa equivalent daily dose (LEDD) decreased over the first year and then stabilised, whereas the entacapone-treated group showed an initial decrease in the first 6-months followed by a dose increase between 7-18-months. Neither COMT inhibitors had significant impact on sleep medication use. CONCLUSION(S): This head-to-head study is the first to demonstrate using 'real-world' data that initiating COMT inhibition with opicapone is likely to decrease the need for post-treatment HCRU versus initiation of COMT inhibition with entacapone. Copyright This article is protected by copyright. All rights reserved.

6. Effects of conventional physical therapy with and without proprioceptive neuromuscular facilitation on balance, gait, and function in patients with Parkinson's disease.

Authors: Mazhar, Tahzeeb; Jameel, Ayesha; Sharif, Faiza and Asghar, Momna

Publication Date: Jun ,2023

Journal: JPMA - Journal of the Pakistan Medical Association 73(6), pp. 1280-1283

Abstract: The study was conducted at University of Lahore Teaching Hospital and Sir Ganga Ram Hospital, Lahore, using non-probability convenience sampling. Thirty-eight patients of Parkinson's disease were allocated by randomisation into two groups. PNF Group (group A) performed proprioceptive neuromuscular facilitation incorporated with conservative treatment, while for the conventional therapy group (group B) only conservative treatment was followed. Berg Balance Scale, Freezing of Gait questionnaire, and Functional Independence measure were used as outcome measuring tool. Berg balance scale values were significantly improved in group A at 12th week as compared to group B. Freezing of gait and functional independence was more significantly reduced in group A at sixth and 12th week as compared to group B. Hence, it is concluded that Proprioceptive neuromuscular facilitation combined with routine treatment regime improves balance, gait, and function of Parkinson's patients more effectively as compared with routine treatment protocol only.

7. Functional roles of reactive astrocytes in neuroinflammation and neurodegeneration

Authors: Patani, Rickie; Hardingham, Giles E. and Liddel, Shane A.

Publication Date: Jul ,2023

Journal: Nature Reviews Neurology 19(7), pp. 395-409

Abstract: Despite advances in uncovering the mechanisms that underlie neuroinflammation and neurodegenerative disease, therapies that prevent neuronal loss remain elusive. Targeting of disease-defining markers in conditions such as Alzheimer disease (amyloid-beta and tau) or Parkinson disease (alpha-synuclein) has been met with limited success, suggesting that these proteins do not act in isolation but form part of a pathological network. This network could involve phenotypic alteration of multiple cell types in the CNS, including

astrocytes, which have a major neurosupportive, homeostatic role in the healthy CNS but adopt reactive states under acute or chronic adverse conditions. Transcriptomic studies in human patients and disease models have revealed the co-existence of many putative reactive sub-states of astrocytes. Inter-disease and even intra-disease heterogeneity of reactive astrocytic sub-states are well established, but the extent to which specific sub-states are shared across different diseases is unclear. In this Review, we highlight how single-cell and single-nuclei RNA sequencing and other 'omics' technologies can enable the functional characterization of defined reactive astrocyte states in various pathological scenarios. We provide an integrated perspective, advocating cross-modal validation of key findings to define functionally important sub-states of astrocytes and their triggers as tractable therapeutic targets with cross-disease relevance. Copyright © 2023. Springer Nature Limited.

8. Hospitalization and the Risk of Initiation of Antipsychotics in Persons With Parkinson's Disease.

Authors: Pirttila, A.;Tiihonen, M.;Paakinaho, A.;Hartikainen, S. and Tolppanen, A. M.

Publication Date: 2023

Journal: Journal of the American Medical Directors Association (pagination), pp. ate of Pubaton: 2023

Abstract: Objectives: The use of antipsychotics in persons with Parkinson's disease (PD) is common, although their use may aggravate the symptoms of PD. Clozapine and quetiapine are the only antipsychotics recommended in PD treatment guidelines. Information on factors associated with initiation of antipsychotics is needed. We investigated whether recent hospitalization is associated with initiation of antipsychotics in persons with PD, and whether discharge diagnoses differ between those who had antipsychotics initiated and those who did not. Design(s): Nested case-control study in the nationwide register-based Finnish Study on Parkinson's disease (FINPARK). Setting and Participants: The FINPARK study includes 22,189 persons who received an incident, clinically verified PD diagnosed during 1996-2015 and were community-dwelling at the time of diagnosis. The cases were 5088 persons who had antipsychotics initiated after PD diagnosis, identified with 1-year washout. The controls were 5088 age-, sex-, and time from PD diagnosis-matched persons who did not use antipsychotics on the matching date (antipsychotic purchase date). Recent hospitalization was defined as discharge in the 2-week period preceding the matching date. Method(s): Associations were investigated with conditional logistic regression. Result(s): Quetiapine was the most commonly initiated antipsychotic (72.0% of cases), followed by risperidone (15.0%). Clozapine was initiated rarely (1.1%). Recent hospitalization associated strongly with antipsychotic initiation [61.2% of cases and 14.9% of controls, odds ratio (OR) 9.42, 95% CI 8.33-10.65], and longer hospitalizations were more common among cases. PD was the most common discharge diagnosis category (51.2% of hospitalized cases and 33.0% controls), followed by mental and behavioral disorders (9.3%) and dementia (9.0%) among cases. Antidementia and other psychotropic medication use were more common among cases. Conclusions and Implications: These results suggest that antipsychotics were initiated because of neuropsychiatric symptoms or aggravation of those symptoms. Antipsychotics should be prescribed after careful consideration to avoid adverse effects in persons with Parkinson's disease. Copyright © 2023 AMDA - The Society for Post-Acute and Long-Term Care Medicine

9. Clinical features and outcomes of hospitalised patients with COVID-19 and Parkinsonian disorders: A multicentre UK-based study.

Authors: Sorrell, Lexy;Leta, Valentina;Barnett, Anton;Stevens, Kara;King, Angela;Inches,

Jemma;Kobylecki, Christopher;Walker, Richard;Chaudhuri, K. Ray;Martin, Hannah;Rideout, Jane;Sneyd, J. Robert;Campbell, Sarah and Carroll, Camille

Publication Date: 2023

Journal: PLoS ONE [Electronic Resource] 18(7), pp. e0285349

Abstract: BACKGROUND: Parkinson's disease has been identified as a risk factor for severe Coronavirus disease 2019 (COVID-19) outcomes. However, whether the significant high risk of death from COVID-19 in people with Parkinson's disease is specific to the disease itself or driven by other concomitant and known risk factors such as comorbidities, age, and frailty remains unclear. OBJECTIVE: To investigate clinical profiles and outcomes of people with Parkinson's disease and atypical parkinsonian syndromes who tested positive for COVID-19 in the hospital setting in a multicentre UK-based study. METHODS: A retrospective cohort study of Parkinson's disease patients with a positive SARS-CoV-2 test admitted to hospital between February 2020 and July 2021. An online survey was used to collect data from clinical care records, recording patient, Parkinson's disease and COVID-19 characteristics. Associations with time-to-mortality and severe outcomes were analysed using either the Cox proportional hazards model or logistic regression models, as appropriate. RESULTS: Data from 552 admissions were collected: 365 (66%) male; median (inter-quartile range) age 80 (74-85) years. The 34-day all-cause mortality rate was 38.4%; male sex, increased age and frailty, Parkinson's dementia syndrome, requirement for respiratory support and no vaccination were associated with increased mortality risk. Community-acquired COVID-19 and co-morbid chronic neurological disorder were associated with increased odds of requiring respiratory support. Hospital-acquired COVID-19 and delirium were associated with requiring an increase in care level post-discharge. CONCLUSIONS: This first, multicentre, UK-based study on people with Parkinson's disease or atypical parkinsonian syndromes, hospitalised with COVID-19, adds and expands previous findings on clinical profiles and outcomes in this population. Copyright: © 2023 Sorrell et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

10. Practical proactive and preventative Parkinson's disease strategies for management in the hospital setting.

Authors: Veilleux Carpentier, Ariane;Salloum, Ramzi G. and Okun, Michael S.

Publication Date: 2023

Journal: Parkinsonism & Related Disorders 113, pp. 105515

11. Establishing a framework for quality of inpatient care for Parkinson's disease: A study on inpatient medication administration.

Authors: Yu, Jeryl Ritzi T.;Sonneborn, Claire;Hogue, Olivia;Ghosh, Debolina;Brooks, Anne;Liao, James;Fernandez, Hubert H.;Shaffer, Shannon;Sperling, Scott A. and Walter, Benjamin L.

Publication Date: 2023

Journal: Parkinsonism & Related Disorders 113, pp. 105491

Abstract: BACKGROUND: The complexity of antiparkinsonian medications makes patients vulnerable to medication deviations. This study examines the frequency and outcomes of

deviations between outpatient and inpatient medication administrations in patients with Parkinson's disease (PD). **METHODS:** We included hospital admissions of patients with PD during a 12-month period at the Cleveland Clinic Main and Fairview campuses. Outpatient regimens were compared with hospital medication administration records to establish rates of deviations in terms of levodopa equivalent daily dose (LEDD) difference, timing deviations/omissions of time-critical medications, substitution of levodopa compounds, and administration of antidopaminergic medications. Logistic regression analyses were used to investigate associations with length of stay (LOS), readmission rates, and mortality. **RESULTS:** The study included 492 patients with 725 admissions. Of those on time-critical medications, 43% had a LEDD deviation and 19% had levodopa formulation substitutions. Of the admission days with known outpatient timing regimens, 47% had an average deviation of more than 30 min and 22% had at least one missed levodopa dose. LOS was longer with each additional day of over-dose (4%), under-dose (14%), missed dose (21%), timing deviation (15%) and substitution (19%), (all p Copyright © 2023. Published by Elsevier Ltd

12. Lipopolysaccharide-binding protein and future Parkinson's disease risk: a European prospective cohort.

Authors: Zhao, Yujia;Walker, Douglas I.;Lill, Christina M.;Bloem, Bastiaan R.;Darweesh, Sirwan K. L.;Pinto-Pacheco, Brismar;McNeil, Brooklyn;Miller, Gary W.;Heath, Alicia K.;Frissen, Myrthe;Petrova, Dafina;Sanchez, Maria-Jose;Chirlaque, Maria-Dolores;Guevara, Marcela;Zibetti, Maurizio;Panico, Salvatore;Middleton, Lefkos;Katzke, Verena;Kaaks, Rudolf;Riboli, Elio, et al

Publication Date: Jul 21 ,2023

Journal: Journal of Neuroinflammation 20(1), pp. 170

Abstract: **INTRODUCTION:** Lipopolysaccharide (LPS) is the outer membrane component of Gram-negative bacteria. LPS-binding protein (LBP) is an acute-phase reactant that mediates immune responses triggered by LPS and has been used as a blood marker for LPS. LBP has recently been indicated to be associated with Parkinson's disease (PD) in small-scale retrospective case-control studies. We aimed to investigate the association between LBP blood levels with PD risk in a nested case-control study within a large European prospective cohort. **METHODS:** A total of 352 incident PD cases (55% males) were identified and one control per case was selected, matched by age at recruitment, sex and study center. LBP levels in plasma collected at recruitment, which was on average 7.8 years before diagnosis of the cases, were analyzed by enzyme linked immunosorbent assay. Odds ratios (ORs) were estimated for one unit increase of the natural log of LBP levels and PD incidence by conditional logistic regression. **RESULTS:** Plasma LBP levels were higher in prospective PD cases compared to controls (median (interquartile range) 26.9 (18.1-41.0) vs. 24.7 (16.6-38.4) microg/ml). The OR for PD incidence per one unit increase of log LBP was elevated (1.46, 95% CI 0.98-2.19). This association was more pronounced among women (OR 2.68, 95% CI 1.40-5.13) and overweight/obese subjects (OR 1.54, 95% CI 1.09-2.18). **CONCLUSION:** The findings suggest that higher plasma LBP levels may be associated with an increased risk of PD and may thus pinpoint to a potential role of endotoxemia in the pathogenesis of PD, particularly in women and overweight/obese individuals. Copyright © 2023. The Author(s)

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