Journal of Drug Assessment ›
Volume 8, 2019 - Issue 1

Open access

936 Views | 12 CrossRef citations to date | 7 Altmetric

Listen

Neurology

Risk factors for impulse control disorders and related behaviors in Parkinson's disease: secondary analyses of the ICARUS study

Paolo Barone, Angelo Antonini, Paolo Stanzione, Karin Annoni, Mahnaz Asgharnejad & Ubaldo Bonuccelli

Pages 159-166 | Received 08 Aug 2019, Accepted 25 Sep 2019, Published online: 25 Oct 2019

Cite this article https://doi.org/10.1080/21556660.2019.1675670 Check for updates

Abstra...

Objectiv... on in patients ... are not fully understo... ...y and post-hoc ... ...0 patients.

Methods ...), ICD incidenc... ...t ICD-positive ... ...he proportio... ...ar 1 or 2), and "ren... ...as also calculate...

Results: Among 709 patients ICD-negative at baseline, 97 screened ICD-positive (13.7%) at year 1. Among 712 patients who were ICD-negative at baseline, 147 were ICD-positive at ≥1 post-baseline visit (20.6%). Among patients who were ICD-negative at baseline who subsequently experienced an ICD, a higher proportion were male or smokers, younger at baseline, younger at disease/symptom onset, and had longer disease duration. Among the whole population, a similar proportion were “new cases” at years 1 (9.7%) and 2 (8.6%) versus the previous visit. The proportion of “remitters” was slightly higher at year 2 (11.0%) than 1 (9.1%) versus previous visit.

Conclusions: The proportion of ICD-remitters approximately matched/exceeded new cases, suggesting patients with ICD are in a state of flux. Current data allow for a conservative estimate of 2-year ICD incidence in ICARUS of ~21% of patients, not accounting for transient new ICD cases between visits.

Keywords:

Impulse control disorders | incidence | Parkinson’s disease | risk factors | predictive factors | ICARUS study

Introd

Over the aviors (altogeth ecognized as a relativ -5. In the publishe sychiatric sympto , one of the large Ds was relativel

ICDs are , with a number ations, depressi ertain personal ecific frontal dysfunct son’s

had more severe non-motor symptoms (including mood and sexual function) and depression, as well as poorer sleep quality and reduced PD-related quality of life compared with those who were ICD-negative[6].

The incidence of ICDs among people with PD is not consistently reported. One single-site study, conducted in small sample size, reported a cumulative ICD incidence of 39.1% during 21 months of dopamine agonist (DA) treatment in PD patients with no previous ICDs; cigarette smoking, caffeine use, motor complications, and higher peak DA use were identified as risk factors[11]. A more recent analysis of data from 320 early-stage PD patients with no prior ICDs from the Parkinson Progression Markers Initiative (PPMI) database reported cumulative incidence of 8% (year 1), 18% (year 2), and 25% (year 3) post-baseline[13]. Younger age at baseline was a risk factor for incident ICD symptoms, while sex, education, and baseline global cognitive performance, anxiety symptoms, depressive symptoms, and motor severity were not significantly associated with incident ICD symptoms[13].

The natural history of ICDs in PD is not clearly established, and few studies report the long-term outcome of interventions for ICDs in PD. Among 12 patients with PD who had discontinued or significantly decreased DA treatment in one long-term follow-up study, 10 (83%) no longer met ICD diagnostic criteria after a mean follow-up period of 29 months[14]. However, ICDs may sometimes be resistant to dopaminergic medication reductio

In order t is importar s along the disease secondary and post lled in the prospect

- Inc
- Risk fa nong patien
- Propor D subtyp e that an analys of interest

Methods

Study design

ICARUS was a prospective, non-interventional, multicenter study in treated Italian outpatients with PD. A detailed description of the ICARUS study design has been published previously[6]. The primary variable was the presence (prevalence and incidence) of overall ICDs and ICD subtypes according to a modified version of the Minnesota Impulsive Disorders Interview (mMIDI)[16]. ICD status was assessed at three study visits: baseline, year 1, and year 2. Switching of patient treatment was permitted at any time during the study, at the discretion of the treating physician.

Measurements

A patient was considered ICD-positive if they answered affirmatively at the mMIDI scale to one gateway question and to one or more of the remaining questions in the same ICD module of the mMIDI interview.

Estimates of ICD incidence

In addition to the point prevalence of ICDs (reported in the primary publication[6]), the planned ICD presence time periods, we have therefor nt new ICD cases oc thus underes

Using culated for patie mMIDI (Table 1)

Table incide

Downlo

- Year 1 (conservative estimate of ICD incidence for year 1);
- Year 1 and/or 2 (conservative estimate of cumulative 2-year ICD incidence).

The number of patients who were ICD-negative at baseline was used as the denominator.

Post-hoc analyses of baseline data according to subsequent ICD status

The large number of patients involved in the ICARUS study permitted meaningful post-hoc examination of baseline data for the subgroup of patients who were negative for ICD at baseline. Patients in this subgroup were further subdivided into “ICD-positive after baseline” (patients who were positive for an ICD at the year 1 and/or year 2 study visits) and “ICD-negative after baseline” (patients who were negative for an ICD at year 1 and year 2 study visits) to identify baseline characteristics that were different between the groups, including:

- Gender, age at baseline, age at PD onset/symptom onset, PD duration, smoking status, alcohol consumption, education level, marital status, employment status, early discontinuation reason, and region of Italy;
- Disease status according to:

1. PD t
2. Func
3. Cogn ssment Batt
4. Beck
5. [illegible]
6. Park
7. Park

Shift in

In additi of “new

to baseline (the latter irrespective of ICD status at year 1). In recognition that ICD status may also reverse, we also report the number and proportion of “remitters” at year 1 relative to baseline, at year 2 relative to year 1, and at year 2 (the latter irrespective of ICD status at year 1) (Table 2).

Table 2. Definition of shift in ICD status at year 1 versus baseline and year 2 versus year 1 or baseline.

Download CSV Display Table

The proportion of “new cases” and “remitters” was calculated as the percentage of the total number of patients assessed at a given visit (i.e. both ICD-positive and -negative).

New cases and remitters were also summarized by baseline characteristics, including gender, age at baseline, age at PD onset, PD duration, and disease status according to PD treatment.

All data were summarized descriptively.

Result

ICD inc

Among t ICD data, 97 scree ICD incidenc

Ther e post-basel e post-baseline imate for cumulat

Analysi

Among p males who

an ICD were younger at baseline, younger at disease and symptom onset, had a longer disease duration, and a greater proportion were smokers compared with those who did not develop an ICD after baseline (Table 3).

Table 3. Baseline characteristics of patients negative for ICD at baseline according to subsequent ICD status at either post-baseline visit (FAS).

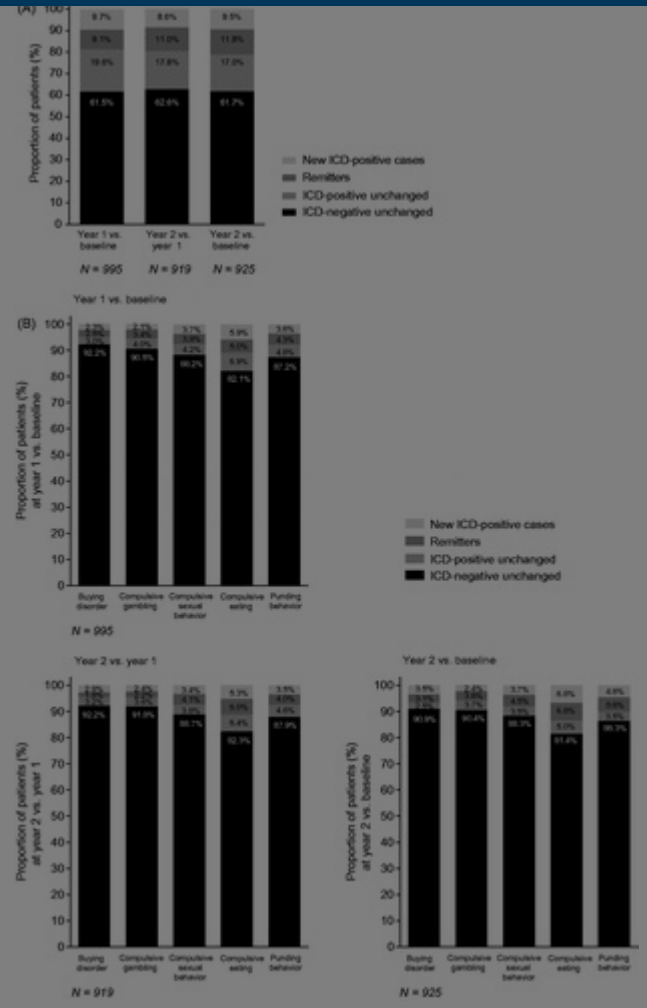
Download CSV Display Table

Baseline severity of PD symptoms and functional disability (HY stage), cognitive function (MMSE, FAB, and PD-CRS), and non-motor symptoms (PD-NMSS total score) were similar between patients who did and did not develop an ICD after baseline (Table 3). However, those who did develop an ICD after baseline had slightly worse depressive symptoms (BDI-II), PD-related health status (PDQ-8), and sleep (PDSS-2) impairment (Table 3).

ICD status: “new cases” and “remitters”

Among the whole population, a similar proportion of patients were considered “new cases” a gure 1(A)). The prop .0%) compare was seen when co cases” and “remitte ous differenc s “remitte

Figu erall ICD behavio ve control disorder ease.

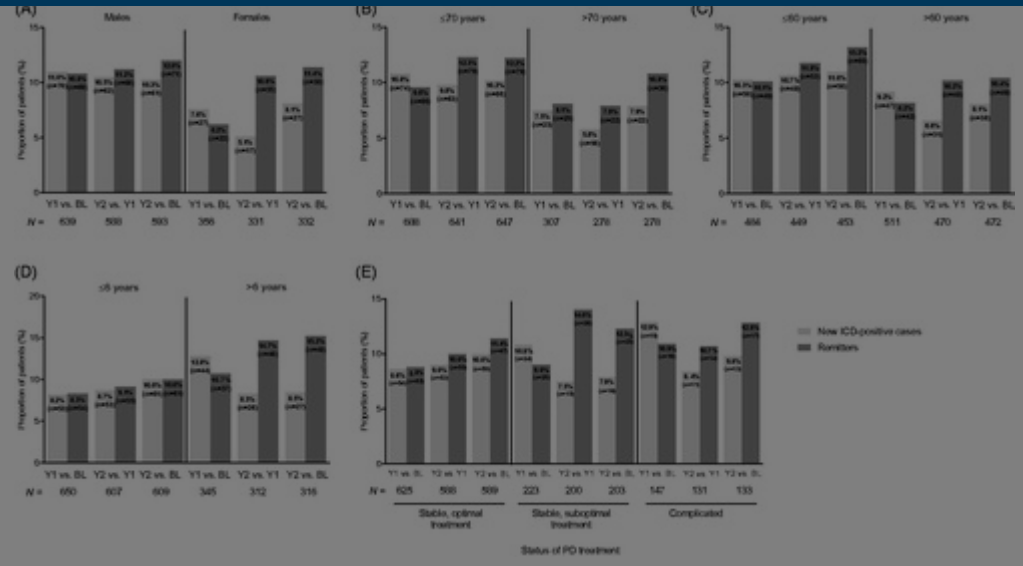


Display full size

ICD status: demographic/clinical features

Analysis cal features indicate g male, younger frequencies of “new

Figure 2 t baseline, (C) age ording to PD treatm sorder; MIDI) ear.



Display full size

The number of “remitters” frequently matched or exceeded the number of “new cases”.

ICD status: ICD behavior subtypes by demographic/clinical features

Examination of ICD behavior subtypes according to demographic and clinical features at baseline among those with shifted ICD status (Table 4) indicated that generally, the numbers of “new cases” and “remitters” were similar or there were more remitters.

Table 4 ICD subtypes (“new cases” and “remitters”) at post-baseli

Downlo

Disc

The subs ggests a 1-year inci ar cumulat are lower than tho 39.1%)[11], but simil PD with no previous ncidence,

Article contents | Related research

given that transient new ICD cases occurring within the year between visits would have remained unrecorded.

The frequency of “new cases” and “remitters” at each visit was also calculated among the whole PD population of the ICARUS study. Whilst the 1-year risk of ICD development among the ICD-negative patients was ~14%, a new ICD case occurred in ~9% of patients each year when considering the whole population (ICD-positive and -negative, regardless of remission status). On average, 10% of patients remitted in a year (9.1% at year 1 vs. baseline and 11.0% at year 2 vs. year 1).

Given that the prevalence of ICDs in the ICARUS study was relatively stable at an average of 28% across the three study visits[6], observed fluctuation of “new cases” and “remitters” suggests that ICDs in PD may be sensitive to treatment adjustments or other factors including dyskinesia[17]; this remains speculative as no such analysis was performed. However, ICD has been shown to peak 4.5 to 5 years after PD treatment initiation[18]. “Remitters” could represent change due to treatment adjustments (either removal of a drug with adverse event or improvement from treatment), as a result of higher disease awareness in the literature and thus better treatment management. Interestingly, among patients who were defined as suboptimal or with complicated PD at baseline, there were more new ICD cases than remitters at year 1; however, at year 2, the pa…tern was reversed, with more remitters than new ICD cases, which may reflect an initia…tment strategy… vALidation of THe u…rapy total dose is a…haviors and dyskines… assess their motor a…spects becaus…

Gene…vious associat…revious research…sk factors for incid…a greater risk, as …previous research…nset ICDs. Being m…SS-2, which

overall quality of sleep), were found to increase the risk for new-onset ICDs in the current study, unlike in the previous studies examining risk factors for incident ICDs[11,13]. Cognitive performance was not predictive of ICD development in the current analysis, consistent with the prior studies, which either showed that global cognitive performance was not significantly associated with incident ICD symptoms[13], or the absolute difference between ICD-positive and ICD-negative groups was small[11]. Some differences in findings across these studies maybe because of the different instruments used to measure PD symptom severity and differences in the methods used to assess risk factors.

This analysis has some limitations. The primary variable of the ICARUS study was the presence (prevalence and incidence) of overall ICDs and ICD subtypes according to mMIDI. Notably, this could be regarded as a surrogate primary variable because the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), was not consistently used for ICD confirmation (as originally planned in the protocol); even so, DSM-IV does not cover all ICD subtypes that occur in patients with PD. Secondly, ICD status was assessed at three study visits (baseline, year 1, and year 2) and not throughout the study period, meaning ICD status between study visits was unknown. Thirdly, treatment could be switched at any time and this was not recorded, which may have influenced the number of “remitters”, with potentially a considerable lag phase of months

is of small numbers

ited, increasi

Conclu

Amon

ximately mat

nd the state is variab

ng PD patients

stimates the true inci

ring within the year

ers are a result of

d patient popula

type

behaviors throughout the disease course and represents an interesting area for future research.

Transparency

Declaration of funding

This study and post-hoc analyses were supported by UCB Pharma, Monheim am Rhein, Germany.

Declaration of financial/other relationships

PB, AA, PS, and UB were study investigators on ICARUS, a UCB Pharma-sponsored study. PB has received personal fees from Acorda Therapeutics, UCB Pharma, and Zambon, and grants from AbbVie, Biotie Therapies, and Zambon. AA has received consultancy fees/honoraria from AbbVie, UCB Pharma, Zambon, Angelini, Lundbeck, Mundipharma, and Medtronic; has served on advisory boards for AbbVie and Acadia; provided expert testimony for Boehringer Ingelheim (pathological gambling cases); and received grants from Neureca Foundation, Gossweiler Foundation, Mundipharma, Italian National Research (project numbers RF-2009-1530177 and RF-2010-2319551), and Horizon2 onoraria from UC for UCB Pharma 013-271966 advisory boards f arma. MA is a former loyment. JDA peer elationships to dis

Author

PB condu analysis, and revi eption, organiza review and

and critique of statistical analysis, and review and critique of manuscript. UB conducted research project conception and execution, review and critique of statistical analysis, and review and critique of manuscript. KA conducted research project conception, organization and execution; review and critique of statistical analysis; and review and critique of manuscript. MA conducted review and critique of statistical analysis and review and critique of manuscript.

Acknowledgements

The authors report this study on behalf of the ICARUS study group (participating sites: A.O. Universitaria Ospedale Policlinico Consorziale, Bari; Istituto Neurologico Mediterraneo NEUROMED, Pozzilli; UOC Neurologia Ospedaliera, Azienda Ospedaliero-Universitaria OO.RR., Foggia; Azienda Ospedaliera Cardinale Giovanni Panico, U. O. di Neurologia, Tricase; ASL MT P.O. Madonna delle Grazie, Matera; A.O. Universitaria Policlinico Tor Vergata, Roma; Dipartimento Scienze Neurologiche Università Degli Studi Federico II, Napoli; Università degli Studi di Roma ‘La Sapienza’ Dipartimento di Scienze Neurologiche, Roma; Policlinico Universitario Gemelli, Roma; IRCCS S. Raffaele Pisana, Roma; UO di Neurologia, Azienda Ospedaliera di Rilievo Nazionale A.Cardarelli, Napoli; A.O. Universitaria Sant'Andrea, Roma; Università di Modena e Reggio Emilia, Ospedale C. Sant'A artimento di Scienze Neurosc Battista-Molinett Universitaria Policlinic e di Neurolog ca, Sassari; Ospedal lentia; Azien Azienda Ospe ULSS 3 Sereniss O. Neurolog cugnano Vicenza; Neurologica I, Padova Universita' Degli St Azienda Ospedal Perugia;

Neuroriabilitazione, Dipartimento di Scienze Neurologiche, Ancona; A.O. Universitaria Careggi Di Firenze, Neurologia I, Ambulatorio Parkinson, Firenze; PO 'SS. Filippo E Nicola' Avezzano, Aquila; Ospedale Nuovo S. Giovanni Di Dio Torregalli, Neurologia, Firenze; Nuovo Ospedale Di Prato Santo Stefano, Neurologia Prato; P.O. Di Summa, Perrino U.O. Neurologia, Brindisi; Ospedale San Giovanni Battista, Roma; IRCCS Istituto C. Besta Disturbi del Movimento, Milano; Centro Parkinson CTO, ASST Nord Milano, Milano; IRCCS Fondazione Istituto Neurologico Casimiro Mondino Di Pavia, Pavia; Ospedale Mauriziano Umberto I Di Torino, Torino; Ospedale Sant'Andrea La Spezia, La Spezia; Presidio Ospedaliero Di Savona, Cairo Montenotte, Savona; Ospedale di Circolo e Fondazione Macchi Varese, Varese; Azienda Sanitaria Universitaria Integrata di Udine, Ospedale Santa Maria della Misericordia, Dipartimento di Neuroscienze, Neurologia, Udine; Ospedale Maggiore Policlinico, Dipartimento di Scienze Neurologiche, Università degli Studi di Milano, Milano; Osp. Maggiore di Modica U.O. Di Neurologia, Ragusa; Azienda Ospedaliera S.Giuseppe Moscati Di Avellin, U.O.C. di Neurologia, A.O.R.N. ‘S.G. Moscati’, Avellino; AOU Pisana, Stabilimento di Santa Chiara, Pisa; Casa di Cura Villa dei Gerani, Catania; Azienda ULSS 3 Serenissima, Ospedale Civile SS Giovanni e Paolo, Neurologia, Venezia; Fondazione Opera San Camillo, Casa di Cura San Pio X, Milano; L’Azienda Ospedaliera di Melegnano-Presidio di 'Vizzolo Predabissi’, Milano; Azienda Ospedaliera Universitaria OO.RR. S.Giovanni di Dio e Ruggi d'Aragona, Salerno; Ospedale Sant'Eugenio, Roma; Ospedale San Filippo Neri, Roma; Istituto Scientifico di Riabilita sità degli Studi di vers in addition S study. The authors ns, London, UK) for w Bauer, MD (UCB Ph Pharma, Brussels nd inter and) for public

Refer

1. Weintraub D, David AS, Evans AH, et al. Clinical spectrum of impulse control disorders in Parkinson's disease. Mov Disord. 2015;30(2):121–127.

PubMed | Web of Science ® | Google Scholar

2. Macphee GJ, Chaudhuri KR, David AS, et al. Managing impulse control behaviours in Parkinson's disease: practical guidelines. Br J Hosp Med. 2013;74(3):160–166.

Web of Science ® | Google Scholar

3. Weintraub D, Koester J, Potenza MN, et al. Impulse control disorders in Parkinson disease: a cross-sectional study of 3090 patients. Arch Neurol. 2010;67(5):589–595.

PubMed | Web of Science ® | Google Scholar

4. Isaias IU, Siri C, Cilia R, et al. The relationship between impulsivity and impulse control disorders in Parkinson's disease. Mov Disord. 2008;23(3):411–415.

PubMed | Web of Science ® | Google Scholar

5. Weintraub D, Hoops S, Shea JA, et al. Validation of the questionnaire for impulsive-compu[illegible]461–1467.

6. Anton[illegible]inical featur[illegible]rosurg Psychi[illegible]

7. Mestr[illegible]ulse control disord[illegible] 2013;[illegible]

8. Weintr[illegible]onist use

973.

PubMed | Google Scholar

9. Weintraub D, Papay K, Siderowf A. Siderowf A for the Parkinson's Progression Markers Initiative. Screening for impulse control symptoms in patients with de novo Parkinson disease: a case-control study. Neurology. 2013;80(2):176–180.

PubMed | Web of Science ® | Google Scholar

10. Brusa L, Pavino V, Massimetti MC, et al. Pathological gambling in Parkinson's disease patients: dopaminergic medication or personality traits fault? J Neurol Sci. 2016;366:167–170.

PubMed | Web of Science ® | Google Scholar

11. Bastiaens J, Dorfman BJ, Christos PJ, et al. Prospective cohort study of impulse control disorders in Parkinson's disease. Mov Disord. 2013;28(3):327–333.

PubMed | Web of Science ® | Google Scholar

12. Santa rol disorders
and c sci
Biobe

13. Smith ms and
dopan sychiatry.
201

14. Mamik se control
disord

15. Kurlan R. Disabling repetitive behaviors in Parkinson's disease. Mov Disord. 2004;19(4):433–437.

PubMed | Web of Science ® | Google Scholar

16. Christenson GA, Faber RJ, de Zwaan M, et al. Compulsive buying: descriptive characteristics and psychiatric comorbidity. J Clin Psychiatry. 1994;55(1):5–11.

PubMed | Web of Science ® | Google Scholar

17. Biundo R, Weis L, Abbruzzese G, et al. Impulse control disorders in advanced Parkinson's disease with dyskinesia: the ALTHEA study. Mov Disord. 2017;32(11):1557–1565.

PubMed | Web of Science ® | Google Scholar

18. Antonini A, Chaudhuri KR, Boroojerdi B, et al. Impulse control disorder related behaviours during long-term rotigotine treatment: a post hoc analysis. Eur J Neurol. 2016;23(10):1556–1565.

PubMed | Web of Science ® | Google Scholar