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Vascular Parkinsonism: Clinical and Imaging Patterns in Diagnostic Definition

Natália Moreira Pacheco

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Professor Doutor Rui Manuel Moreira Araújo

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Doutora Rita Sofia Silva Nunes da Cruz Rato

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Vascular Parkinsonism: Clinical and Imaging Patterns in Diagnostic Definition

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Eu, Natália Moreira Pacheco, abaixo assinado, nº mecanográfico 201905284, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro que:

☒ Não procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* para nenhuma das tarefas no contexto do meu trabalho de Dissertação ou Monografia

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DEDICATÓRIA

Gostaria de começar por agradecer aos meus pais, Natália e António, por todo o apoio, confiança e carinho constantes. Foram eles que, dia após dia, me relembraram das minhas capacidades, mesmo nos momentos em que a incerteza falava mais alto, e que garantiram que conseguisse chegar ao fim deste percurso.

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Article Title: Vascular Parkinsonism: Clinical and Imaging Patterns in Diagnostic Definition

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ABSTRACT

Background: Vascular parkinsonism (VaP) is a heterogeneous clinical entity characterised by parkinsonian features attributed to cerebrovascular disease, typically identified through neuroimaging. In recent years, the validity of the term "vascular parkinsonism" has been increasingly debated by leading experts in neurodegenerative disorders. Differentiating it from other conditions, particularly idiopathic Parkinson's disease (IPD), remains clinically challenging due to overlapping manifestations and the absence of disease-specific biomarkers. Accurate diagnostic distinction is essential to guide appropriate treatment strategies and align therapeutic interventions with the underlying aetiology.

Objective: This study aims to characterise and compare the clinical and neuroradiological features of patients with VaP and IPD, with particular emphasis on the topography and extent of cerebrovascular lesions.

Methods: A cross-sectional study was conducted involving 14 patients with VaP and 58 with IPD, all followed at a tertiary movement disorders centre. Demographic and clinical data were retrospectively extracted from electronic medical records. Neuroimaging exams were independently reviewed by a neuroradiologist blinded to clinical diagnosis. Statistical analyses were subsequently performed to compare groups.

Results: VP patients were significantly older ($p<0.001$) and had a higher prevalence of vascular risk factors ($p=0.05$). Clinically, they showed a predominance of lower-limb parkinsonism ($p<0.001$), postural instability ($p=0.003$), falls ($p<0.001$), freezing of gait ($p=0.002$), and corticospinal ($p=0.006$) or pseudobulbar signs ($p=0.036$). Levodopa responsiveness was minimal or absent in 71.4% of VP cases, in contrast to 89.7% of patients with IPD who demonstrated a robust therapeutic response ($p<0.001$).

Neuroimaging revealed moderate-to-severe white matter hyperintensities (Fazekas grades 2–3) in 71.4% of VaP patients, compared with only 3.4% in the IPD group ($p<0.001$). Strategic infarcts were exclusively identified in patients with VP ($p<0.001$).

Conclusions: These findings reinforce the clinicoradiological distinction between VaP and IPD. Hallmark features of VP include predominant lower-body involvement, postural instability, poor dopaminergic responsiveness, and a substantial cerebrovascular burden on neuroimaging. While no single feature is pathognomonic, the integration of clinical and radiological data remains essential for accurate diagnosis. Future research should aim to validate diagnostic criteria and explore biomarker-based approaches.

Keywords: Vascular parkinsonism; Idiopathic Parkinson's disease; Cerebrovascular disease; Neuroimaging; White matter hyperintensities**.**

INTRODUCTION

Vascular Parkinsonism (VaP), a subtype of secondary parkinsonism, is a neurodegenerative condition characterized by clinical features that overlap with idiopathic Parkinson's disease (IDP). However, its underlying pathophysiology and aetiology are distinct [1].

While IPD typically arises from dopaminergic neuronal loss in the substantia nigra [2], VaP is associated with cerebrovascular disease and vascular risk factors, particularly hypertension. This leads to a heterogeneous pattern of ischemic damage in brain regions that modulate motor function [3]. These lesions may include strategic subcortical infarcts, diffuse white matter ischaemic lesions, and, more rarely, large vessel infarcts affecting the basal ganglia [3,4,5]. Differentiating between the two conditions is clinically challenging due to shared motor manifestations, including bradykinesia, rigidity, and postural instability. However, VaP may be present with an atypical clinical signature and

distinct neuroimaging features that could facilitate its differentiation from IPD [6]. Moreover, IPD may coexist with cerebrovascular disease, which is an expected finding given the age-related rise in the prevalence of both conditions, further complicating diagnostic accuracy [7].

Clinically, VaP is often characterized by lower-body parkinsonism, with predominant gait disturbances, including shuffling, freezing of gait (FOG), and early postural instability. Additionally, cognitive decline, pseudobulbar symptoms, and pyramidal signs may coexist, reflecting multifocal vascular involvement. Notably, VaP show poor to no levodopa response, further supporting its distinct nosology [8,9,10]. Despite VaP's growing recognition, its clinical distinction from IPD remains inherently challenging. Currently, no pathognomonic clinical features reliably differentiate both entities, making diagnostic decisions and therapeutic approaches largely subjective. Consequently, dopaminergic therapy is frequently employed, despite the limited high-quality evidence supporting its efficacy in this context [11].

Neuroimaging, particularly magnetic resonance imaging (MRI), plays a crucial role in identifying structural vascular lesions that may contribute to the development of parkinsonism. The most typical radiological findings include multiple lacunar infarcts, cerebral microbleeds, white matter hyperintensities (WMHs) suggestive of small vessel disease (SVD), enlargement of perivascular spaces, and ischemic lesions in critical motor pathways [8,12]. Nevertheless, the absence of a standardized imaging definition for VaP significantly limits diagnostic consistency, and conventional MRI findings may overlap with those observed in IPD, especially in elderly populations with concomitant vascular burden [11]. Lately, advanced imaging techniques, such as diffusion tensor imaging [13], functional imaging like positron emission tomography [14], and single-photon emission computed tomography [15] have revealed some potential in refining the diagnostic

accuracy by highlighting the vascular contributions to parkinsonism and supporting its differentiation from neurodegenerative aetiologies. Additionally, the classification of VaP has also been questioned [16]. On the one hand, WMHs observed on MRI not being exclusively attributable to vascular causes may, for instance, result from age-related degeneration [17]. On the other hand, VaP appears to be a rare cause of parkinsonism despite the high frequency of basal ganglia and white matter infarcts in the elderly [18]. Furthermore, clinical and pathological parallels between VaP Binswanger's disease have led some authors to propose a shared disease spectrum, characterized by overlapping symptomatology and therapeutic strategies [19]. Finally, some authors have proposed a network of brain regions where vascular damage could lead to the development of parkinsonism, from the motor cortex to the striatum and subthalamic nucleus. It would be important to confirm in other cohorts whether patients with VaP or IPD have cerebrovascular damage predominantly within this brain network [20]. It is a mysterious and poorly understood topic, with some authors even questioning the existence of VaP as an entirely distinct entity [16].

Given the complexity of VaP, this study aims to describe the clinical and neuroradiological picture of a cohort of patients diagnosed with IPD and VaP, with particular focus on the extent and topography of vascular lesions in each group.

METHODS

Selection and Description of Participants

A cross-sectional study was conducted, including 14 patients diagnosed with VaP and 58 patients with IPD. Participants were consecutively selected from the Movement Disorders outpatient clinic at the Neurology Department of Unidade Local de Saúde São João, where they were regularly followed by specialized neurologists between December 2022

and December 2024. At the time of data collection, each patient had a diagnosis of VaP or IPD, based on clinical presentation and neuroimaging findings, and in accordance with official guidelines [3,21]. The cohort had been followed longitudinally for a median duration of 4.0 ± 5.0 years.

Inclusion criteria required patients to be adults and to have a diagnosis of (1) VaP, according to the updated expert recommendations and Zijlmans criteria for the Clinical Diagnosis of VaP [3], or (2) IPD, based on the Movement Disorder Society Clinical Diagnostic Criteria for Parkinson's Disease [21]. Exclusion criteria included the following: (1) diagnosis of atypical or genetic parkinsonian syndromes; (2) any other identifiable cause of secondary parkinsonism (e.g., drug-induced); (3) coexisting neurological or orthopaedic conditions significantly impairing gait or mimicking parkinsonian features; (4) presence of neurodegenerative comorbidities that could confound motor or cognitive symptomatology; and (5) inability to undergo neuroimaging assessment by either computerized tomography (CT) or MRI. Data collection was conducted from December 2024 to March 2025.

Demographic and Clinical Data

Demographic and clinical data were collected retrospectively from electronic medical records. The following variables were recorded: age, sex, weight, height, diagnosis (VaP or IPD), age at symptom onset, duration of follow-up, and presence of cardiovascular risk factors (including hypertension, dyslipidaemia, smoking, diabetes mellitus, and alcohol consumption). Additional comorbidities, such as atrial fibrillation and obstructive sleep apnoea syndrome, were also documented. The clinical onset of parkinsonism was categorized as (1) acute or subacute onset, defined as emergence of parkinsonism ≤1 year after a stroke; or (2) chronic, indicating insidious onset of parkinsonism over the years [3].

The parkinsonian motor phenotype was classified as akinetic-rigid, tremor-dominant, mixed (akinetic-rigid and tremor), or postural instability and gait disorder (PIGD). For all patients, the presence of motor and non-motor features was assessed, including lower-limb predominance, FOG, falls, postural instability, gait disturbances, resting tremor, cogwheel rigidity, bradykinesia, corticospinal and cerebellar signs, bulbar symptoms, visual hallucinations, and urinary incontinence. Motor severity and dopaminergic responsiveness were evaluated using the Movement Disorders Society's Unified Parkinson's Disease Rating Scale part III (MDS-UPDRS-III) [22] and the modified Hoehn and Yahr staging [23]. Assessments were conducted at various stages of disease progression and included patients in both "ON" and "OFF" medication states, depending on the timing of routine clinical evaluations. The presence of lower-limb parkinsonism predominance was defined by a ≥2-point difference between upper and lower-limb scores of bradykinesia and rigidity (from MDS-UPDRS-III). Clinical asymmetry was defined as the absolute difference between the summed motor scores for the right and left extremities (items 3.3–3.8 and 3.15–3.17), with a threshold of ≥2 points used to indicate clinically meaningful asymmetry, in accordance with previous studies [24].

Neuroimaging Data

Structural neuroimaging (CT or MRI, depending on availability) was reviewed by a neuroradiologist who was blinded to the clinical diagnosis. All IPD patients underwent brain MRI, while VaP patients were evaluated using either MRI or CT. Image interpretation followed STRIVE recommendations [12]. The following imaging variables were included in the analysis: (1) WMHs were assessed using the Fazekas visual scale (grades 0–3), based on T2-weighted or FLAIR sequences (MRI) or equivalent hypodensities on CT, where applicable; (2) ischemic or haemorrhagic lesions in critical

motor pathways (binary variable: present/absent) were defined as lacunes of presumed vascular origin or enlarged perivascular spaces located in strategic subcortical regions involved in motor control, namely the internal capsule, putamen, caudate and globus pallidus. These included both ischemic and post-haemorrhagic changes, regardless of size. In some cases, prominent perivascular spaces located in these regions were also considered potentially relevant, based on their topography and possible impact on motor pathways; and (3) strategic infarcts were defined as visible lesions affecting clinically relevant anatomical locations associated with an increase in basal ganglia motor output or decrease of thalamocortical drive, according to Zijlmans criteria for the Clinical Diagnosis of VaP [3]. Lesions were documented by presence and location without volumetric quantification.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics, version 30.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to characterize the study population. Continuous variables were summarised as mean ± standard deviation or median ± interquartile range, according to distribution assessed by the Shapiro–Wilk test. Categorical variables were reported as frequencies and percentages. Comparisons between the VaP and IPD groups were performed using the Student's t-test or Mann–Whitney U test for continuous variables and the Pearson's chi-square test or Fisher's exact test for categorical variables, as appropriate. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Demographic Characteristics

A total of 72 cases, 14 VaP patients and 58 IPD patients, were included in this study. From an initial cohort of 492 screened patients, the following exclusions were applied: 144 patients lacked available neuroimaging studies; 113 had atypical, genetic, or other secondary forms of parkinsonism; 163 were diagnosed with movement disorders unrelated to parkinsonism (e.g., essential tremor). The VaP and IPD sample had a median follow-up duration of 3.00 ± 4.00 and 5.00 ± 7.00 years, respectively. Patients diagnosed with VaP were significantly older than those with IPD, with mean ages of 79.6 ± 6.0 and 71.8 ± 8.2 years, respectively (p<0.001). The groups were matched regarding sex. The mean BMI was 25.10 ± 3.68 in the VaP group and 25.84 ± 3.72 in the IDP group, with no statistically significant difference between them (p=0.558). Vascular risk factors were more frequently present among VaP patients. Arterial hypertension was significantly more prevalent in the VaP group (92.9% vs 63.8%, p=0.05), while other vascular risk factors, such as diabetes mellitus (p=0.645), dyslipidaemia (p=0.332), smoking (p=1.000), and alcohol consumption (p=0.438), did not differ significantly between groups. Additionally, regarding obstructive sleep apnea syndrome and atrial fibrillation no statistical difference was found between groups (p=0.248 and 0.180, respectively) (**Table *1***).

Clinical Features and Levodopa Responsiveness

The mean age of onset was significantly higher in the VaP group compared to the IPD group (73.82 ± 4.98 vs. 63.00 ± 8.82 years; p<0.001). Also, clinical onset patterns showed substantial divergence. Acute or subacute onset occurred in 64.3% of VaP patients, compared to just 3.4% of those with IPD (p<0.001). Motor phenotype distribution also differed: PIGD subtype predominated in VaP (78.6%), while it was less common among

IPD patients (6.9%, $p<0.001$). IPD patients more frequently presented with asymmetry and classic parkinsonian signs such as cogwheel rigidity (91.4% vs. 42.9%, $p<0.001$) and resting tremor (69.0% vs. 28.6%, $p=0.005$), whereas VaP cases showed a significantly higher prevalence of lower-limb predominance (50.0% vs. 0%, $p<0.001$), FOG (57.1% vs. 10.3%, $p=0.002$), falls (78.6% vs. 10.3%, $p<0.001$), and postural instability (85.7% vs. 43.1%, $p=0.004$). On the Hoehn and Yahr scale, patients with VaP were significantly more likely to present with more advanced disease stages compared to those with IPD ($p<0.001$). Specifically, 85.7% of VaP patients were in stages 3.0–5.0, whereas only 31.0% of IPD patients fell into this category. Conversely, stages 1.0–2.5 were more frequent in IPD patients (69.0%) compared to VaP (14.3%). The MDS-UPDRS-III scores were higher in the VaP group (32.14 ± 16.12 points) compared to the IPD group (25.40 ± 11.32 points), although this difference did not reach statistical significance ($p=0.071$). Corticospinal and bulbar signs were more common in VaP, representing a statistically significant difference ($p=0.006$ and 0.036, respectively). Urinary incontinence was also more frequently reported in VaP patients, a difference that approached but did not reach statistical significance (42.9% vs. 17.2%, $p=0.068$). Response to levodopa differed markedly between groups ($p<0.001$). A full response was observed in 89.7% of IPD patients, compared to none in the VaP group. The majority of VaP patients (85.7%) exhibited no response, while 14.3% demonstrated a partial response. In contrast, only 6.9% of IPD patients failed to respond, and 3.4% showed a partial response (**Table *2***).

Neuroimaging Data

Radiological findings (**Table *3***) demonstrated a clear divergence between groups. Moderate-to-severe WMHs, defined as Fazekas grade 2–3, were identified in 71.4% of

VaP patients, with 57.1% exhibiting grade 3 confluent lesions. Conversely, 79.3% of IPD patients had either no lesions or only punctate foci (Fazekas grade 0–1), with only one reaching grade 3 (p<0.001). Strategic infarcts, namely those involving the thalamic ventrolateral nucleus (TVL) (28.6%) (**Figure *1***) or medial frontal cortex (7.1%), were found exclusively in the VaP group (35.7%, p<0.001). Lesions affecting critical motor pathways (internal capsule, putamen, caudate or globus pallidus) were more prevalent in VaP (57.1% vs. 29.3%), although this difference did not reach statistical significance (p=0.064).

We further explored the relationship between the extent of WMHs, as graded by the Fazekas scale, and clinical manifestations across the entire cohort, regardless of the diagnostic label (IPD or VaP) (**Table *4***). Our results show that, compared to those with mild lesions, patients with moderate-to-severe lesions showed significantly less motor asymmetry (p<0.001), resting tremor (p=0.071) and cogwheel rigidity (p=0.016), and a higher prevalence of lower-limb predominance (p<0.001), postural instability (p=0.002) and falls (p<0.001). Corticospinal signs, bulbar features, and urinary incontinence also appeared more frequently in the higher Fazekas group, although these differences did not reach statistical significance (p=0.219, 0.090 and 0.070, respectively).

VaP Cases Description

Detailed examination of individual VaP cases (**Table *5***) confirmed the syndrome's heterogeneity. The most frequent pattern was insidious onset with chronic progression (50%), followed by subacute onset (35.7%), and only two cases (14.3%) reported an acute presentation of hemibody syndrome suggestive of strategic stroke involvement. Clinically, lower-limb predominance was observed in 57.1% the patients, and postural instability affected 85.7% of cases. Falls occurred in 78.6% of cases, and FOG in 57.1%.

Resting tremor was noted in 28.6% of VaP patients, although in all these cases, it was either asymmetrical or associated with hemiparkinsonism. Non-motor features such as urinary incontinence (42.9%), corticospinal signs (21.4%), and bulbar symptoms (14.3%) were also recorded, further supporting diffuse subcortical involvement. Levodopa responsiveness was minimal or absent in 71.4% of VaP cases, with only 28.6% patients exhibiting a partial motor improvement.

Radiologically, all patients exhibited WMHs, with 71.4% classified as Fazekas grade 2–3 and 57.1% reaching grade 3. Strategic infarcts were identified in 5 patients (35.7%). Additionally, 57.1% of patients harboured lacunar infarcts or lacunae caused by enlarged perivascular spaces in critical motor pathways. Two patients lacked any discrete infarcts in strategic or motor-relevant territories but still exhibited extensive confluent WMHs.

DISCUSSION

In this cohort, we analysed 72 cases, 14 with VaP and 58 with IPD, to explore the presence of distinguishing clinical and neuroimaging features. Our findings highlight key differentiating characteristics between VaP and IPD, reinforcing and extending existing knowledge on their respective phenotypic profiles.

Prevalence and Demographic Profile

In our specialized outpatient setting for movement disorders, VaP accounted for 4.3% of all parkinsonism cases, aligning with the reported prevalence of 2.5–5% in the literature [25]. However, after application of inclusion and exclusion criteria, VaP patients represented 19.4% of the final study sample. Patients with VaP were significantly older at symptom onset, consistent with previous studies identifying advanced age and hypertension as major risk factors [1,6]. Hypertension was markedly more prevalent in

this group, reinforcing its established role as a major risk factor in cerebrovascular disease and subsequent dysfunction of the basal ganglia thalamocortical network [26,27]. While diabetes mellitus and dyslipidaemia were also common, their association was less pronounced, highlighting the multifactorial vascular risk profile typical of VaP patients. These findings advocate for targeted cardiovascular risk factor management strategies in elderly populations to potentially mitigate disease onset and progression [19,26].

Clinical Features and Phenotypic Profile

Clinically, VaP patients exhibited a marked lower-body predominance of parkinsonian features. Gait disturbance, freezing episodes, frequent falls, and marked postural instability were often observed. Upper body involvement was less pronounced and usually symmetric in VaP, whereas IPD patients typically presented with asymmetrical upper-limb onset characteristic of Parkinson's disease [2]. Notably, resting tremor was absent or minimal in most VaP cases, in contrast to IPD. Consistent with this, prior observations have likewise reported that VaP patients have a higher frequency of lower-body predominance, worse axial (gait/postural) impairment, rare or absent resting tremor, and a more symmetrical presentation compared to IPD patients [7,8,9,11,19]. Accordingly, the majority of VaP cases had a PIGD motor subtype, whereas IPD patients more often exhibited akinetic-rigid or tremor-dominant phenotypes. Furthermore, VaP patients frequently exhibited corticospinal tract signs (e.g., hyperreflexia, Babinski sign), pseudobulbar features, and urinary incontinence, reflecting pyramidal and subcortical involvement. These features also emphasize VaP as a syndrome of diffuse motor system disruption, rather than a pure basal ganglia degenerative process [28].

Temporal Evolution and Subtypes

The pattern of symptom onset further distinguished the two groups. Most IPD patients had a gradual, insidious onset of motor symptoms, typical of a neurodegenerative process [2]. In contrast, a subset of VaP patients presented with an acute or subacute onset of parkinsonian signs that were temporally associated with a cerebrovascular event, corresponding to the acute post-stroke subtype of VaP [28]. In our series, two cases presented with acute hemiparkinsonism following lacunar infarcts in the lenticulostriate territory, consistent with VaP due to the disruption of post-synaptic basal ganglia structures. However, the majority of VaP cases in our cohort exhibited an insidious course without evidence of a temporal or anatomical cause, aligning with the SVD-subtype of VaP, attributed primarily to chronic ischemic damage to frontal-subcortical circuits rather than discrete strategic infarctions [26-28].

Levodopa Responsiveness

Our findings reinforce the limited dopaminergic responsiveness in VaP patients compared to the vast majority of IPD patients, a key discriminator that has been regarded as a hallmark of this entity in literature [1,7]. In our cohort, all patients with VaP underwent an empirical trial of levodopa at adequate dosages. However, objective motor assessments and clinical evaluations demonstrated none or only minimal improvement in 71.4% of cases. Quantitatively, a recent review established that only about one-third of patients meeting VaP criteria showed any appreciable levodopa response [29]. This therapeutic disparity reflects distinct underlying pathophysiological mechanisms. In IPD, degeneration of nigrostriatal dopaminergic neurons, results in marked motor improvement with dopamine replacement. In contrast, in VaP, the basal ganglia dopamine terminals are often intact, but downstream frontal-subcortical circuits are disrupted by

ischemia, rendering dopamine replacement much less effective [7,11]. Nonetheless, some heterogeneity in levodopa response was observed between VaP phenotypes. Three patients with subacute post-stroke VaP, characterized by focal infarcts involving the TVL nucleus, exhibited partial motor improvement with dopaminergic therapy, likely reflecting a concomitant upstream nigrostriatal pathway dysfunction and/or residual thalamocortical drive. In contrast, those with confluent leukoaraiosis-driven VaP showed minimal to no therapeutic response, reinforcing the concept that VaP, particularly the SVD-subtype, is characteristically refractory to dopaminergic treatment. Collectively, our findings support the increasingly accepted view that VaP represents a heterogeneous clinical entity [9], suggesting that a spectrum exists and that an occasional overlap or coexistent nigrostriatal degeneration can occur, with some patients benefiting from dopaminergic therapy [29]. However, the overall poor response remains a significant clinical marker separating VaP from IPD.

Neuroimaging Findings

Almost all VaP patients exhibited significant cerebrovascular pathology on neuroimaging, including multiple lacunar infarcts in subcortical structures and chronic ischemic changes. In contrast, MRIs from IPD patients were frequently unremarkable or revealed only nonspecific changes.

The burden of cerebrovascular injury was significantly greater in the VaP group, particularly diffuse WMHs compatible with SVD. Most VaP patients demonstrated moderate-to-severe WMHs, corresponding to Fazekas grades 2–3, whereas nearly all IPD patients had none or only mild changes (Fazekas grades 0–1). This radiological contrast aligns with previous studies identifying confluent leukoaraiosis and multiple lacunes as hallmark features of VaP. For instance, a case-control reported Fazekas grade ≥2 in 93%

of VaP, compared to only 12.5% of patients with IPD [8]. Similarly, prior studies have reported abnormal structural neuroimaging in 90–100% of VaP patients versus 12–43% in IPD [4]. These findings, however, should be interpreted within the broader context of cerebrovascular aging. Mild WMHs are common in elderly individuals and are often linked to vascular risk factors and cognitive decline, but not necessarily become a direct pathogenic correlate of parkinsonism [30]. This was evident in our IPD group, where mild WMHs were frequent but not explanatory of the motor phenotype. One study reported significantly more subcortical infarcts and confluent WMHs in VaP patients than in age-matched individuals with IPD, reinforcing the pathological distinction [3]. Interestingly, one IPD patient showed extensive WMHs, making the distinction from VaP less clear. However, the clinical presentation of gradual asymmetrical onset favoured IPD over VaP. Despite the PIGD phenotype presentation, the age at onset was relatively low (68 years), and there was evident dopaminergic response. Vascular risk factors were present, which may explain the imaging findings. Nonetheless, a mixed presentation of IPD and SVD cannot be excluded [28,31].

Beyond diffuse ischemic changes, a subset of VaP patients in our cohort presented with strategic infarcts directly decreasing thalamocortical drive, especially focal strokes in critical motor circuits such as the TVL and medial frontal cortex. Moreover, another subset developed acute onset hemiparkinsonism following white matter lacunar infarction in the lenticulostriate topography. These cases illustrate a mechanistically distinct form of VaP in which a single lesion is sufficient to produce parkinsonism by disrupting key components of the motor pathway. Similarly, autopsy studies observed that a subset of autopsy-confirmed VaP cases had macroscopic lacunar infarcts in the basal ganglia or thalamus associated with acute contralateral hemiparkinsonism, distinguishing them from

those with diffuse SVD [3]. However, in our study, no infarcts in or near areas that can increase the basal ganglia motor output were detected.

Importantly, no MRI pattern is pathognomonic for VaP. While confluent periventricular WMHs were a consistent feature among VaP patients in our study, similar changes were occasionally observed in elderly IPD patients, highlighting that leukoaraiosis is neither specific to VaP nor invariably pathogenic [30]. As such, neuroimaging findings must be interpreted in conjunction with the clinical presentation; although they can strongly support a diagnosis of VaP when aligned with clinical features, they are insufficient on their own to definitively distinguish VaP from IPD or other parkinsonian disorders.

VaP Cases Description

Analysis of individual VaP cases highlights the importance of clinicoradiological correlation and the heterogeneity of VaP subtypes. One case exhibiting a focal strategic infarct in the medial frontal cortex, along with unilateral parkinsonism, gait impairment, and concomitant hemiparesis, corticospinal tract signs, and pseudobulbar signs, suggests coexistent damage to corticospinal and corticobulbar fibers in the internal capsule. Two additional patients with lacunar infarcts within the lenticulostriate territory, particularly involving the posterior putamen, exhibited asymmetric motor symptoms, including cogwheel rigidity and resting tremor. These findings suggest that lesions in the dorsolateral putamen may shift the balance of basal ganglia output toward the indirect pathway, contributing to tremor and rigidity [3]. Four other patients exhibited focal strategic infarcts involving the TVL nucleus, with a subacute onset of predominantly asymmetrical parkinsonism. In all these cases, the lesion's topography corresponded closely with the clinical presentation, and three patients showed partial response to levodopa. These cases are consistent with the post-stroke VaP subtype, in which infarcts

disrupt key motor pathways, occasionally preserving sufficient postsynaptic integrity to allow dopaminergic responsiveness. Nonetheless, the presence of classical IPD features, such as unilateral onset, resting tremor, and partial levodopa response, suggests a potential overlap in clinical phenotypes. This raises the question of whether vascular pathologies may blur the phenotypic boundaries between IPD and VaP. In fact, mixed phenotypes within the VaP spectrum have been increasingly recognized and acknowledged as "mixed VaP/IPD subtype" [31]. These challenging cases with same-side pyramidal and parkinsonian signs and new-onset contralateral lesions affecting motor pathways also raise the question – are clinicians overdiagnosing parkinsonism in patients with pyramidal slowness, as some authors have suggested? [16]. Future studies with blinded clinician evaluation might be important to answer these questions.

The majority of VaP cases did not have a single strategic infarct and instead showed a diffuse burden of SVD, with multiple lacunes and confluent WMHs (Fazekas grade 2–3). Clinically, these patients followed an insidious course, characterized by symmetrical lower-body parkinsonism, postural instability, frequent falls, urinary symptoms, corticospinal tract signs, and a poor response to levodopa, features typical of the classic SVD-driven VaP phenotype. In these cases, the neuroimaging findings of extensive leukoaraiosis and widespread subcortical injury were congruent with the diffuse motor symptoms observed, including frontal gait disorder and pseudobulbar features [32].

Diagnostic Implications and Imaging Considerations

Our findings emphasize the need for clinicoradiological coherence to support VaP diagnosis. Neuroimaging evidence must align with the clinical picture. When discrepancies are present, including cases of unexpected levodopa responsiveness or isolated tremor without corresponding vascular lesions, alternative or coexisting

diagnoses should be considered. In diagnostically uncertain situations, dopamine transporter imaging (DaTSCAN) serves as a valuable tool: while patients with VaP, particularly those without direct nigrostriatal infarcts, often exhibit normal findings due to preserved presynaptic dopaminergic neurons, a pathological scan with reduced striatal uptake is typical of IPD [15].

Recognizing strategic vascular lesions on neuroimaging is essential, as they carry distinct therapeutic and prognostic implications. Unlike IPD's progressive course, VaP may stabilize or fluctuate with effective management of vascular risk factors. Consequently, treatment should prioritize vascular risk management, secondary stroke prevention, and rehabilitation, rather than escalating dopaminergic therapy in non-responsive VaP cases [19,29]. Misdiagnosis in either direction risks depriving patients of appropriate treatment, whether by exposing VaP patients to unnecessary medication and side effects, or by withholding effective symptomatic therapy from IPD patients.

Study Limitations and Future Directions

This study has limitations that warrant consideration. First, the sample size, particularly for the VaP group (N=14), was small, which limits statistical power and may reduce the generalizability of findings. Although this reflects the low prevalence of VaP it restricts the detection of subtle intergroup differences. The absence of multivariate analysis also prevented adjustment for potential confounders. Moreover, the retrospective and cross-sectional design relied on routine clinical records, resulting in heterogeneous data collection, particularly in neurocognitive assessments, which were not systematically analysed due to missing data. This restricts the comparative analysis of neurocognitive impairment between groups. Furthermore, no causal inferences can be made about the temporal relationship between vascular lesions and parkinsonian features. While

associations between WMHs and clinical phenotype were observed, we cannot determine whether these vascular changes preceded symptom onset or represent age-related comorbidity. Additionally, although diagnostic criteria based on neuropathological findings are the most widely accepted, the lack of standardized diagnostic criteria for VaP limits comparison between clinical studies in this field. Internationally validated definitions are urgently needed to ensure consistency and methodological rigor. Also, an overlap between vascular and degenerative pathologies cannot be excluded, with autopsy studies revealing coexisting Lewy body pathology and cerebrovascular lesions in older adults [33]. Incorporating advanced biomarkers and functional imaging into algorithms may enhance future diagnostic precision. In addition, the use of visual rating scales for imaging may lack the sensitivity of advanced quantitative or connectivity-based analyses. Finally, our study was single-centred and conducted in a tertiary movement disorders centre, introducing potential referral bias and limiting external validity.

Future research should aim to validate diagnostic models in multicentre, longitudinal cohorts, incorporating advanced neuroimaging, molecular biomarkers, and vascular risk profiling. Such studies are critical to clarify the natural history of VaP, its response to vascular risk modification, and the development of personalized therapeutic strategies beyond dopaminergic replacement.

CONCLUSION

This study reinforces the clinical heterogeneity of VaP and its overlap with IPD and other gait disorders. Although distinguishing features were identified, none of these, individually, is pathognomonic for VaP. While extensive WMHs were frequent among VaP patients and likely contributes to gait dysfunction, the degree of leukoaraiosis does not consistently associate with parkinsonian severity, suggesting that additional

mechanisms, such as coexisting nigrostriatal degeneration, may be involved. The absence of universally accepted diagnostic criteria and disease-specific biomarkers continues to limit diagnostic certainty. Differential diagnoses, including IPD with coincidental vascular changes, normal pressure hydrocephalus, or atypical parkinsonian syndromes, should be carefully considered, particularly in ambiguous cases.

Authors defend that the term “vascular parkinsonism” likely incorporates a spectrum of distinct pathophysiological entities. Currently, only a minority of cases, such as those with infarcts involving directly the substantia nigra or the nigrostriatal pathway, can be confidently classified as “definite” VaP. Future research should prioritise the refinement of diagnostic criteria to enhance diagnostic accuracy and create more effective management strategies for this uncommon but clinically significant parkinsonian syndrome.

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DECLARATIONS

Ethics Approval and Consent to Participate

This study was approved by the Local Ethics Committee of Unidade Local de Saúde São João. Written informed consent was not obtained from participants.

Consent for Publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to institutional and ethical constraints regarding patient confidentiality but are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Source of Funding

No funding was received for this study.

Authors' Contributions

NMP and RSSNCR were responsible for data acquisition, analysis, and interpretation. CCR and MBSSP conducted the neuroradiological analysis and interpretation. RMMA and RSSNCR substantively revised the manuscript. RMMA and CLS conceptualized and supervised the study. All authors reviewed and approved the final manuscript.

TABLES AND FIGURES

Table 1 – Demographic and clinical characteristics of patients with Vascular Parkinsonism and Idiopathic Parkinson's Disease

	VaP (N=14)	**IDP** (N=58)	
Characteristics	**n (%)**	**n (%)**	***p*-value**
Age (mean ± SD)	79.50 ± 6.28	71.98 ± 8.20	<0.001†
Sex			0.645
Male	8 (57.1)	37 (63.8)	
Female	6 (42.9)	21 (36.2)	
Body Mass Index	24.85 ± 3.78	25.87 ± 3.69	0.433†
Hypertension	13 (92.9)	37 (63.8)	0.05*
Dyslipidaemia	14 (100)	51 (87.9)	0.332*
Diabetes	7 (50.0)	20 (34.5)	0.282
Obstructive Sleep Apnea Syndrome	2 (14.3)	3 (5.2)	0.248*
Atrial Fibrillation	3 (21.4)	5 (8.6)	0.180*
Smoking	3 (21.4)	15 (25.9)	1.000*
Alcohol	3 (21.4)	8 (13.8)	0.438*

SD – Standard deviation. * – *p*-value using the Fisher's exact test; † – *p*-value using the Student's t-test.

Table 2 – Comparison of Disease and Motor Characteristics between Patients with Vascular Parkinsonism and Idiopathic Parkinson's Disease

	VaP (N=14)	IDP (N=58)	
Characteristics	**n (%)**	**n (%)**	***p*-value**
Age Of Onset (mean ± SD)	73.20 ± 4.78	63.36 ± 9.07	<0.001†
Follow-Up Duration (median ± IQR)	3.00 ± 4.00	5.00 ± 7.00	0.914‡
Clinical Onset			<0.001*
Acute or Subacute	7 (50.0)	0 (0.0)	
Chronic	7 (50.0)	58 (100)	
Hoehn and Yahr Scale			<0.001
1.0–2.5	2 (14.3)	40 (69.0)	
3.0–5.0	12 (85.7)	18 (31.0)	
MDS-UPDRS-III	29.50 ± 13.62	26.47 ± 11.59	0.057†
Disease Phenotype			<0.001*
Akinetic-Rigid	0 (0.0)	24 (41.4)	
Tremor-Dominant	0 (0.0)	16 (27.6)	
Mixed	3 (21.4)	14 (24.1)	
PIGD	11 (78.6)	4 (6.9)	
Motor Symptoms			
Asymmetry	5 (35.7)	42 (72.4)	0.014*
Lower-Limb Predominance	7 (50.0)	0 (0.0)	<0.001*
Freezing of Gait	8 (57.1)	6 (10.3)	0.002*
Falls	11 (78.6)	6 (10.3)	<0.001*
Postural Instability	12 (85.7)	24 (41.4)	0.003
Gait Alterations	14 (100)	44 (75.9)	0.057*
Resting Tremor	4 (28.6)	40 (69.0)	0.005
Cogwheel Rigidity	6 (42.9)	53 (91.4)	<0.001*
Bradykinesia	14 (100)	58 (100)	–
Corticospinal Signs	3 (21.4)	0 (0.0)	0.006*
Bulbar Signs	2 (14.3)	0 (0.0)	0.036*
Visual Hallucinations	1 (7.1)	5 (8.6)	1.000*
Urinary Incontinence	6 (42.9)	10 (17.2)	0.068*
Levodopa Response			<0.001*
Response	0 (0.0)	52 (89.7)	
No Response	10 (71.4)	4 (6.9)	
Partial Response	4 (28.6)	2 (3.4)	

SD – Standard deviation; IQR – Interquartile range; MDS-UPDRS-III – Movement Disorders Society's Unified Parkinson's Disease Rating Scale part III; PIGD – Postural instability and gait disorder. * – *p*-value using the Fisher's exact test; † – *p*-value using the Student's t-test; ‡ – *p*-value using the Mann-Whitney U test.

Table 3 – Neuroimaging characteristics between patients with Vascular Parkinsonism and Idiopathic Parkinson's Disease

	VaP (N=14)	**IDP** (N=58)	
Characteristics	**n (valid %)**	**n (valid %)**	***p*-value**
Fazekas Score			<0.001*
0 – No Lesions	0 (0.0)	10 (17.2)	
1 – Punctate Lesions	4 (28.6)	36 (62.1)	
2 – Beginning Confluence	2 (14.3)	11 (19.0)	
3 – Extensive Confluent Areas	8 (57.1)	1 (1.7)	
Ischemic Haemorrhagic Lesions in Critical Motor Pathways	7 (50.0)	16 (27.6)	0.122*
Strategic Lesion			<0.001*
None	9 (64.3)	58 (100)	
Medial Frontal Cortex	1 (7.1)	0 (0.0)	
Thalamic Ventrolateral nucleus	4 (28.6)	0 (0.0)	

* – *p*-value using the Fisher's exact test

Table 4 – Patient distribution by white-matter lesion burden (Fazekas scale: 0–1 = mild; 2–3 =moderate-to-severe)

	Fazekas 0–1 (N=50)	**Fazekas 2–3** (N=22)	
Characteristics	**n (valid %)**	**n (valid %)**	***p*-value**
Asymmetry	39 (78.0)	8 (36.4)	<0.001
Lower-Limb Predominance	0 (0.0)	7 (31.8)	<0.001*
Freezing of Gait	6 (12.0)	8 (36.4)	0.024*
Falls	6 (12.0)	11 (50.0)	<0.001
Postural Instability	19 (38.0)	17 (77.3)	0.002
Gait Alterations	37 (74.0)	21 (95.5)	0.050*
Resting Tremor	34 (68.0)	10 (45.5)	0.071
Cogwheel Rigidity	45 (90.0)	14 (63.6)	0.016*
Corticospinal Signs	1 (2.0)	2 (9.1)	0.219*
Bulbar Signs	0 (0.0)	2 (9.1)	0.090*
Urinary Incontinence	8 (16.0)	8 (36.4)	0.070*

* – *p*-value using the Fisher's exact test

Table 5 – Clinical and Neuroimaging Profile of Patients with Vascular Parkinsonism

Age	Sex	Onset	Motor Symptoms/Signs	Non-Motor Features	Levodopa Response	Exam	Fazekas Scale	Strategic Lesions	Motor Pathway Lesion
83	M	Subacute	Bk + PI + Falls + CogR	None	Partial	MRI	2	TVL	Yes
84	M	Subacute	Bk + PI + Falls + CogR (asymmetric)	None	Partial	CT	1	TVL	Yes
73	M	Subacute	Bk + PI + FOG + Falls + CogR + RT (asymmetric)	None	Partial	CT	1	TVL	No
78	M	Subacute	Bk + PI + CogR + RT (asymmetric)	UI	No	CT	3	TVL	Yes
76	F	Subacute	Bk + LLP + PI + FOG + Falls + hemiparesis	UI CSS BS	No	MRI	2	Medial Frontal Cortex	Yes
86	F	Acute	Bk + CogR + RT (hemiparkinsonism)	None	No	CT	1	No	Yes
88	F	Acute	Bk + CogR + RT (hemiparkinsonism)	None	No	MRI	1	No	Yes
89	M	Chronic	Bk + LLP + PI + FOG + Falls	UI CSS	No	CT	3	No	No
93	M	Chronic	Bk + LLP + PI + Falls	BS	No	CT	3	No	No
88	M	Chronic	Bk + LLP + PI + FOG + Falls	None	No	MRI	3	No	No
79	M	Chronic	Bk + LLP + PI + FOG + Falls	UI	Partial	CT	3	No	Yes
76	F	Chronic	Bk + LLP + PI + FOG + Falls	UI	No	MRI	3	No	No
67	F	Chronic	Bk + LLP + PI + FOG + Falls	UI	No	MRI	3	No	Yes
77	F	Chronic	Bk + LLP + PI + FOG + Falls	None	No	MRI	3	No	No

M – Male; F – Female; Bk – Bradykinesia; LLP – Lower-limb predominance; FOG – Freezing of gait; PI – Postural instability; RT – Resting tremor; CogR – Cogwheel rigidity; CSS – Corticospinal signs; UI – Urinary incontinence; BS – Bulbar signs.; TVL – Thalamic ventrolateral nucleus; CT – Computed tomography; MRI – Magnetic resonance imaging.

Figure 1 – Bilateral, well-defined hyperintense lesions in both thalami on a FLAIR sequence, consistent with chronic lacunar infarcts, are observed in both thalami. Given their topography, potentially involving the ventrolateral thalamic nuclei, these may represent strategic lesions disrupting thalamocortical motor pathways. In the context of the patient's atypical parkinsonism, such lesions fulfill the criteria proposed by Zijlmans et al. (Mov Disord. 2004;19(6):630–640) for VaP, which include damage to regions that reduce thalamocortical drive.

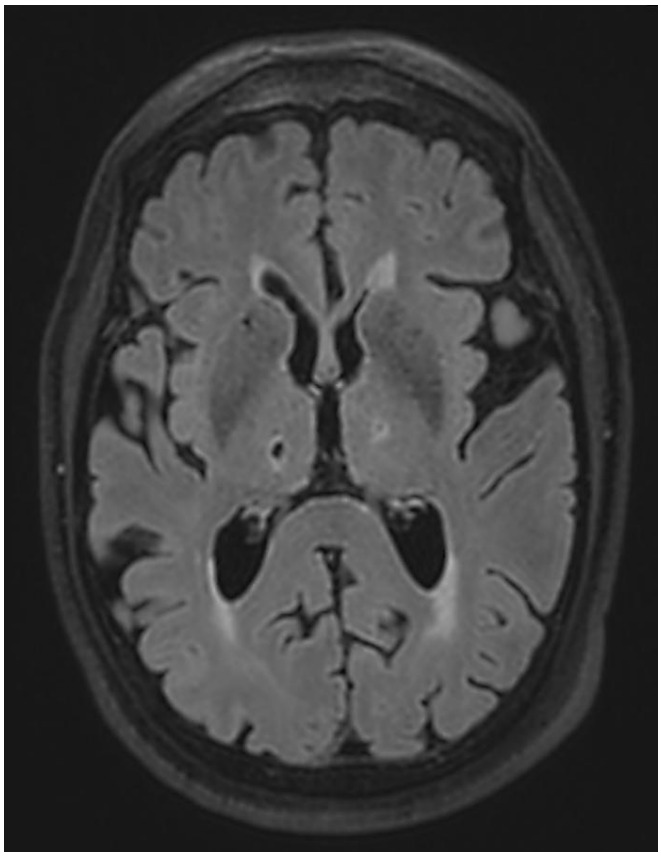

Figure 1 – Bilateral hyperintense lesions in both thalami on a FLAIR sequence.

APPENDICES:

- Reporting guidelines (STROBE for cross-sectional studies)
- BMC Neurology formatting guidelines
- Authorisation by the Hospital Ethics Committee

STROBE Statement – Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	**Page 2:** "A cross-sectional study was conducted involving 14 patients with VaP and 58 with IPD, all followed at a tertiary movement disorders centre."
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	**Pages 2 and 3:** "Methods: A cross-sectional study was conducted involving 14 patients with VaP and 58 with IPD, all followed at a tertiary movement disorders centre. Demographic and clinical data were retrospectively extracted from electronic medical records. Neuroimaging exams were independently reviewed by a neuroradiologist blinded to clinical diagnosis. Statistical analyses were subsequently performed to compare groups. Results: VP patients were significantly older ($p<0.001$) and had a higher prevalence of vascular risk factors ($p=0.05$). Clinically, they showed a predominance of lower-limb parkinsonism ($p<0.001$), postural instability ($p=0.003$), falls ($p<0.001$), freezing of gait ($p=0.002$), and corticospinal ($p=0.006$) or pseudobulbar signs ($p=0.036$). Levodopa responsiveness was minimal or absent in 71.4% of VP cases, in contrast to 89.7% of patients with IPD who demonstrated a robust therapeutic response ($p<0.001$). Neuroimaging revealed moderate-to-severe white matter hyperintensities (Fazekas grades 2–3) in 71.4% of VaP patients, compared with only 3.4% in the IPD group ($p<0.001$). Strategic infarcts were exclusively identified in patients with VP ($p<0.001$). Conclusions: These findings reinforce the clinicoradiological distinction between VaP and IPD."
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	**Page 3:** "Vascular Parkinsonism (VaP), a subtype of secondary parkinsonism, is a neurodegenerative condition characterized by clinical features that overlap with idiopathic Parkinson's disease (IDP)." **Page 4:** "Despite VaP's growing recognition, its clinical distinction from IPD remains inherently challenging. Currently, no pathognomonic clinical features reliably differentiate both entities, making diagnostic decisions and therapeutic approaches largely subjective." **Page 4:** "Nevertheless, the absence of a standardized imaging definition for VaP significantly limits diagnostic consistency, and conventional MRI findings may overlap with those observed in IPD, especially in elderly populations with concomitant vascular burden." **Page 5:** "Additionally, the classification of VaP has also been questioned [16]. On the one hand, WMHs observed on MRI not being exclusively attributable to vascular causes may, for instance, result from age-related

			degeneration [17]. On the other hand, VaP appears to be a rare cause of parkinsonism despite the high frequency of basal ganglia and white matter infarcts in the elderly [18]. Furthermore, clinical and pathological parallels between VaP Binswanger's disease have led some authors to propose a shared disease spectrum, characterized by overlapping symptomatology and therapeutic strategies [19]. Finally, some authors have proposed a network of brain regions where vascular damage could lead to the development of parkinsonism, from the motor cortex to the striatum and subthalamic nucleus. It would be important to confirm in other cohorts whether patients with VaP or IPD have cerebrovascular damage predominantly within this brain network [20]. It is a mysterious and poorly understood topic, with some authors even questioning the existence of VaP as an entirely distinct entity."
Objectives	3	State specific objectives, including any prespecified hypotheses	**Page 5:** "Given the complexity of VaP, this study aims to describe the clinical and neuroradiological picture of a cohort of patients diagnosed with IPD and VaP, with particular focus on the extent and topography of vascular lesions in each group."
Methods			
Study design	4	Present key elements of study design early in the paper	**Page 5:** "A cross-sectional study was conducted, including 14 patients diagnosed with VaP and 58 patients with IPD. " **Page 6:** "At the time of data collection, each patient had a diagnosis of VaP or IPD, based on clinical presentation and neuroimaging findings, and in accordance with official guidelines [3,21]."
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	**Page 5:** "Participants were consecutively selected from the Movement Disorders outpatient clinic at the Neurology Department of Unidade Local de Saúde São João, where they were regularly followed by specialized neurologists between December 2022 and December 2024." **Page 6:** "The cohort had been followed longitudinally for a median duration of 4.0 ± 5.0 years. (…) Data collection was conducted from December 2024 to March 2025."
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	**Page 6:** "Inclusion criteria required patients to be adults and to have a diagnosis of (1) VaP, according to the updated expert recommendations and Zijlmans criteria for the Clinical Diagnosis of VaP [3], or (2) IPD, based on the Movement Disorder Society Clinical Diagnostic Criteria for Parkinson's Disease [21]. Exclusion criteria included the following: (1) diagnosis of atypical or genetic parkinsonian syndromes; (2) any other identifiable cause of secondary parkinsonism (e.g., drug-induced); (3) coexisting neurological or orthopaedic conditions significantly impairing gait or mimicking parkinsonian features; (4) presence of neurodegenerative comorbidities

			that could confound motor or cognitive symptomatology; and (5) inability to undergo neuroimaging assessment by either computerized tomography (CT) or MRI."
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	**Pages 6 and 7:** "The following variables were recorded: age, sex, weight, height, diagnosis (VaP or IPD), age at symptom onset, duration of follow-up, and presence of cardiovascular risk factors (including hypertension, dyslipidaemia, smoking, diabetes mellitus, and alcohol consumption). Additional comorbidities, such as atrial fibrillation and obstructive sleep apnoea syndrome, were also documented. The clinical onset of parkinsonism was categorized as (1) acute or subacute onset, defined as emergence of parkinsonism ≤1 year after a stroke; or (2) chronic, indicating insidious onset of parkinsonism over the years [3]. The parkinsonian motor phenotype was classified as akinetic-rigid, tremor-dominant, mixed (akinetic-rigid and tremor), or postural instability and gait disorder (PIGD). For all patients, the presence of motor and non-motor features was assessed, including lower-limb predominance, FOG, falls, postural instability, gait disturbances, resting tremor, cogwheel rigidity, bradykinesia, corticospinal and cerebellar signs, bulbar symptoms, visual hallucinations, and urinary incontinence." **Pages 7 and 8:** "The following imaging variables were included in the analysis: (1) WMHs were assessed using the Fazekas visual scale (grades 0–3), based on T2-weighted or FLAIR sequences (MRI) or equivalent hypodensities on CT, where applicable; (2) ischemic or haemorrhagic lesions in critical motor pathways (binary variable: present/absent) were defined as lacunes of presumed vascular origin or enlarged perivascular spaces located in strategic subcortical regions involved in motor control, namely the internal capsule, putamen, caudate and globus pallidus. These included both ischemic and post-haemorrhagic changes, regardless of size. In some cases, prominent perivascular spaces located in these regions were also considered potentially relevant, based on their topography and possible impact on motor pathways; and (3) strategic infarcts were defined as visible lesions affecting clinically relevant anatomical locations associated with an increase in basal ganglia motor output or decrease of thalamocortical drive, according to Zijlmans criteria for the Clinical Diagnosis of VaP [3]."
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment	**Page 6:** "Demographic and clinical data were collected retrospectively from electronic medical records." **Page 7:** "Motor severity and dopaminergic responsiveness were evaluated using the Movement Disorders Society's Unified Parkinson's Disease Rating Scale part III (MDS-UPDRS-III) [22] and the modified Hoehn and Yahr staging [23]. Assessments were conducted at various stages of disease progression and included patients in both "ON" and "OFF" medication

		methods if there is more than one group	states, depending on the timing of routine clinical evaluations. The presence of lower-limb parkinsonism predominance was defined by a ≥2-point difference between upper and lower-limb scores of bradykinesia and rigidity (from MDS-UPDRS-III). Clinical asymmetry was defined as the absolute difference between the summed motor scores for the right and left extremities (items 3.3–3.8 and 3.15–3.17), with a threshold of ≥2 points used to indicate clinically meaningful asymmetry." **Pages 7 and 8:** "Structural neuroimaging (CT or MRI, depending on availability) was reviewed by a neuroradiologist who was blinded to the clinical diagnosis. All IPD patients underwent brain MRI, while VaP patients were evaluated using either MRI or CT. Image interpretation followed STRIVE recommendations [12]. (…) Lesions were documented by presence and location without volumetric quantification."
Bias	9	Describe any efforts to address potential sources of bias	**Page 6:** "At the time of data collection, each patient had a diagnosis of VaP or IPD, based on clinical presentation and neuroimaging findings, and in accordance with official guidelines [3,21]." **Page 7:** "Structural neuroimaging (CT or MRI, depending on availability) was reviewed by a neuroradiologist who was blinded to the clinical diagnosis."
Study size	10	Explain how the study size was arrived at	A sample size calculation was not performed. The study included all eligible patients available within the predefined time frame, reflecting a convenience sample based on clinical records from a tertiary movement disorders clinic. This approach is consistent with the retrospective and exploratory nature of the study.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	**Page 8:** "Continuous variables were summarised as mean ± standard deviation or median ± interquartile range, according to distribution assessed by the Shapiro–Wilk test."
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	**Page 8:** "All statistical analyses were conducted using IBM SPSS Statistics, version 30.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to characterize the study population. Continuous variables were summarised as mean ± standard deviation or median ± interquartile range, according to distribution assessed by the Shapiro–Wilk test. Categorical variables were reported as frequencies and percentages. Comparisons between the VaP and IPD groups were performed using the Student's t-test or Mann–Whitney U test for continuous variables and the Pearson's chi-square test or Fisher's exact test for categorical variables, as appropriate.

			A p-value of ≤ 0.05 was considered statistically significant."
		(*b*) Describe any methods used to examine subgroups and interactions	**Page 8:** "Comparisons between the VaP and IPD groups were performed using the Student's t-test or Mann–Whitney U test for continuous variables and the Pearson's chi-square test or Fisher's exact test for categorical variables, as appropriate."
		(*c*) Explain how missing data were addressed	All included patients had complete clinical and neuroimaging data relevant to the study objectives. Missing data were not a significant issue and did not require imputation.
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Not applicable. All eligible cases were included consecutively from the institutional database, without the use of probabilistic or complex sampling techniques. Therefore, no analytical adjustments related to sampling strategy were required.
		(*e*) Describe any sensitivity analyses	Not applicable. No sensitivity analyses were performed.
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	**Page 9:** "A total of 72 cases, 14 VaP patients and 58 IPD patients, were included in this study. The VaP and IPD sample had a median follow-up duration of 3.00 ± 4.00 and 5.00 ± 7.00 years, respectively."
		(b) Give reasons for non-participation at each stage	**Page 9:** "From an initial cohort of 492 screened patients, the following exclusions were applied: 144 patients lacked available neuroimaging studies; 113 had atypical, genetic, or other secondary forms of parkinsonism; 163 were diagnosed with movement disorders unrelated to parkinsonism (e.g., essential tremor)."
		(c) Consider use of a flow diagram	Not performed.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and	**Page 9:** "Patients diagnosed with VaP were significantly older than those with IPD, with mean ages of 79.6 ± 6.0 and 71.8 ± 8.2 years, respectively (p<0.001). The groups were matched regarding sex. The mean BMI was 25.10 ± 3.68 in the VaP group and 25.84 ± 3.72 in the IDP group, with no statistically significant difference between them (p=0.558). Vascular risk factors were more frequently present among VaP patients. Arterial

		potential confounders	hypertension was significantly more prevalent in the VaP group (92.9% vs 63.8%, p=0.05), while other vascular risk factors, such as diabetes mellitus (p=0.645), dyslipidaemia (p=0.332), smoking (p=1.000), and alcohol consumption (p=0.438), did not differ significantly between groups. Additionally, regarding obstructive sleep apnea syndrome and atrial fibrillation no statistical difference was found between groups (p=0.248 and 0.180, respectively) (Table 1)."
		(b) Indicate number of participants with missing data for each variable of interest	All included patients had complete clinical and neuroimaging data relevant to the study objectives. Missing data were not a significant issue and did not require imputation.
Outcome data	15*	Report numbers of outcome events or summary measures	**Pages 9–11:** "The mean age of onset was significantly higher in the VaP group compared to the IPD group (73.82 ± 4.98 vs. 63.00 ± 8.82 years; p<0.001). Also, clinical onset patterns showed substantial divergence. Acute or subacute onset occurred in 64.3% of VaP patients, compared to just 3.4% of those with IPD (p<0.001). Motor phenotype distribution also differed: PIGD subtype predominated in VaP (78.6%), while it was less common among IPD patients (6.9%, p<0.001). IPD patients more frequently presented with asymmetry and classic parkinsonian signs such as cogwheel rigidity (91.4% vs. 42.9%, p<0.001) and resting tremor (69.0% vs. 28.6%, p=0.005), whereas VaP cases showed a significantly higher prevalence of lower-limb predominance (50.0% vs. 0%, p<0.001), FOG (57.1% vs. 10.3%, p=0.002), falls (78.6% vs. 10.3%, p<0.001), and postural instability (85.7% vs. 43.1%, p=0.004). On the Hoehn and Yahr scale, patients with VaP were significantly more likely to present with more advanced disease stages compared to those with IPD (p<0.001). Specifically, 85.7% of VaP patients were in stages 3.0–5.0, whereas only 31.0% of IPD patients fell into this category. Conversely, stages 1.0–2.5 were more frequent in IPD patients (69.0%) compared to VaP (14.3%). The MDS-UPDRS-III scores were higher in the VaP group (32.14 ± 16.12 points) compared to the IPD group (25.40 ± 11.32 points), although this difference did not reach statistical significance (p=0.071). Corticospinal and bulbar signs were more common in VaP, representing a statistically significant difference (p=0.006 and 0.036, respectively). Urinary incontinence was also more frequently reported in VaP patients, a difference that approached but did not reach statistical significance (42.9% vs. 17.2%, p=0.068). Response to levodopa differed markedly between groups (p<0.001). A full response was observed in 89.7% of IPD patients, compared to none in the VaP group. The majority of VaP patients (85.7%) exhibited no response, while 14.3% demonstrated a partial response. In contrast, only 6.9% of

			IPD patients failed to respond, and 3.4% showed a partial response (Table 2). (…) Radiological findings (Table 3) demonstrated a clear divergence between groups. Moderate-to-severe WMHs, defined as Fazekas grade 2–3, were identified in 71.4% of VaP patients, with 57.1% exhibiting grade 3 confluent lesions. Conversely, 79.3% of IPD patients had either no lesions or only punctate foci (Fazekas grade 0–1), with only one reaching grade 3 ($p<0.001$). Strategic infarcts, namely those involving the thalamic ventrolateral nucleus (TVL) (28.6%) (Figure 1) or medial frontal cortex (7.1%), were found exclusively in the VaP group (35.7%, $p<0.001$). Lesions affecting critical motor pathways (internal capsule, putamen, caudate or globus pallidus) were more prevalent in VaP (57.1% vs. 29.3%), although this difference did not reach statistical significance ($p=0.064$). We further explored the relationship between the extent of WMHs, as graded by the Fazekas scale, and clinical manifestations across the entire cohort, regardless of the diagnostic label (IPD or VaP) (Table 4). Our results show that, compared to those with mild lesions, patients with moderate-to-severe lesions showed significantly less motor asymmetry, resting tremor and cogwheel rigidity, and a higher prevalence of lower-limb predominance, postural instability and falls. Corticospinal signs, bulbar features, and urinary incontinence also appeared more frequently in the higher Fazekas group, although these differences did not reach statistical significance." **Page 11:** "Detailed examination of individual VaP cases (Table 5) confirmed the syndrome's heterogeneity." **Pages 28–32 (Tables 1–5)**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Not applicable. All estimates were unadjusted. Between-group comparisons were performed using appropriate univariate statistical tests (e.g., Mann–Whitney U test, chi-square or Fisher's exact test), without adjustment for potential confounders. No multivariable models were applied, given the exploratory nature and limited sample size. **Page 19:** "The absence of multivariate analysis also prevented adjustment for potential confounders."
		(*b*) Report category boundaries when continuous variables were categorized	**Page 6:** "The clinical onset of parkinsonism was categorized as (1) acute or subacute onset, defined as emergence of parkinsonism ≤1 year after a stroke; or (2) chronic, indicating insidious onset of parkinsonism over the years." **Page 7:** "The presence of lower-limb parkinsonism predominance was defined by a ≥2-point difference

			between upper and lower-limb scores of bradykinesia and rigidity (from MDS-UPDRS-III). Clinical asymmetry was defined as the absolute difference between the summed motor scores for the right and left extremities (items 3.3–3.8 and 3.15–3.17), with a threshold of ≥2 points used to indicate clinically meaningful asymmetry." **Pages 29 and 31 (Tables 2 and 4):** Although not explicitly detailed in the main text, Hoehn and Yahr stages were grouped as "1.0–2.5" (early stages without postural instability) and "3.0–5.0" (advanced stages with postural instability) for statistical comparison. Similarly, the Fazekas score was categorised as "0–1" (mild white matter changes) and "2–3" (moderate-to-severe) in the analysis.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable. The study did not involve the calculation of relative risks or risk estimates over time, as it focused on cross-sectional group comparisons rather than outcome prediction or incidence modelling.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	A subgroup analysis was performed comparing clinical features between patients with Fazekas scores 0–1 versus 2–3. No formal interaction or sensitivity analyses were conducted. **Page 11:** "We further explored the relationship between the extent of WMHs, as graded by the Fazekas scale, and clinical manifestations across the entire cohort, regardless of the diagnostic label (IPD or VaP) (Table 4). Our results show that, compared to those with mild lesions, patients with moderate-to-severe lesions showed significantly less motor asymmetry ($p<0.001$), resting tremor ($p=0.071$) and cogwheel rigidity ($p=0.016$), and a higher prevalence of lower-limb predominance ($p<0.001$), postural instability ($p=0.002$) and falls ($p<0.001$). Corticospinal signs, bulbar features, and urinary incontinence also appeared more frequently in the higher Fazekas group, although these differences did not reach statistical significance ($p=0.219$, 0.090 and 0.070, respectively)."
Discussion			
Key results	18	Summarise key results with reference to study objectives	**Page 12:** "In this cohort, we analysed 72 cases, 14 with VaP and 58 with IPD, to explore the presence of distinguishing clinical and neuroimaging features. Our findings highlight key differentiating characteristics between VaP and IPD, reinforcing and extending existing knowledge on their respective phenotypic profiles."
Limitations	19	Discuss limitations of the study, taking into	**Pages 19 and 20:** "This study has limitations that warrant consideration. First, the sample size, particularly for the VaP group (N=14), was small, which limits statistical

		account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	power and may reduce the generalizability of findings. Although this reflects the low prevalence of VaP it restricts the detection of subtle intergroup differences. The absence of multivariate analysis also prevented adjustment for potential confounders. Moreover, the retrospective and cross-sectional design relied on routine clinical records, resulting in heterogeneous data collection, particularly in neurocognitive assessments, which were not systematically analysed due to missing data. This restricts the comparative analysis of neurocognitive impairment between groups. Furthermore, no causal inferences can be made about the temporal relationship between vascular lesions and parkinsonian features. While associations between WMHs and clinical phenotype were observed, we cannot determine whether these vascular changes preceded symptom onset or represent age-related comorbidity. Additionally, although diagnostic criteria based on neuropathological findings are the most widely accepted, the lack of standardized diagnostic criteria for VaP limits comparison between clinical studies in this field. Internationally validated definitions are urgently needed to ensure consistency and methodological rigor. Also, an overlap between vascular and degenerative pathologies cannot be excluded, with autopsy studies revealing coexisting Lewy body pathology and cerebrovascular lesions in older adults [32]. Incorporating advanced biomarkers and functional imaging into algorithms may enhance future diagnostic precision. In addition, the use of visual rating scales for imaging may lack the sensitivity of advanced quantitative or connectivity-based analyses."
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	**Pages 20 and 21:** "This study reinforces the clinical heterogeneity of VaP and its overlap with IPD and other gait disorders. Although distinguishing features were identified, none of these, individually, is pathognomonic for VaP. While extensive WMHs were frequent among VaP patients and likely contributes to gait dysfunction, the degree of leukoaraiosis does not consistently associate with parkinsonian severity, suggesting that additional mechanisms, such as coexisting nigrostriatal degeneration, may be involved. The absence of universally accepted diagnostic criteria and disease-specific biomarkers continues to limit diagnostic certainty. Differential diagnoses, including IPD with coincidental vascular changes, normal pressure hydrocephalus, or atypical parkinsonian syndromes, should be carefully considered, particularly in ambiguous cases. Authors defend that the term "vascular parkinsonism" likely incorporates a spectrum of distinct pathophysiological entities. Currently, only a minority of cases, such as those with infarcts involving directly the substantia nigra or the nigrostriatal pathway, can be confidently classified as "definite" VaP. Future research should prioritise the refinement of diagnostic criteria to enhance diagnostic accuracy and create more effective

			management strategies for this uncommon but clinically significant parkinsonian syndrome."
Generalisability	21	Discuss the generalisability (external validity) of the study results	**Pages 19 and 20:** "This study has limitations that warrant consideration. First, the sample size, particularly for the VaP group (N=14), was small, which limits statistical power and may reduce the generalizability of findings. Although this reflects the low prevalence of VaP it restricts the detection of subtle intergroup differences. (…) our study was single-centred and conducted in a tertiary movement disorders centre, introducing potential referral bias and limiting external validity. Future research should aim to validate diagnostic models in multicentre, longitudinal cohorts, incorporating advanced neuroimaging, molecular biomarkers, and vascular risk profiling. Such studies are critical to clarify the natural history of VaP, its response to vascular risk modification, and the development of personalized therapeutic strategies beyond dopaminergic replacement."
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Not applicable. **Page 27:** "No funding was received for this study."

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMC Neurology

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Only articles, clinical trial registration records and abstracts that have been published or are in press, or are available through public e-print/preprint servers, may be cited.

Unpublished abstracts, unpublished data and personal communications should not be included in the reference list, but may be included in the text and referred to as "unpublished observations" or "personal communications" giving the names of the involved researchers. Obtaining permission to quote personal communications and unpublished data from the cited colleagues is the responsibility of the author. Only footnotes are permitted. Journal abbreviations follow Index Medicus/MEDLINE.

Any in press articles cited within the references and necessary for the reviewers' assessment of the manuscript should be made available if requested by the editorial office.

How to format your references

Please check the Instructions for Authors for the relevant journal and article type for examples of the relevant reference style.

Web links and URLs: All web links and URLs, including links to the authors' own websites, should be given a reference number and included in the reference list rather than within the text of the manuscript. They should be provided in full, including both the title of the site and the URL, as well as the date the site was accessed, in the following format: The Mouse Tumor Biology Database. http://tumor.informatics.jax.org/mtbwi/index.do. Accessed 20 May 2013. If an author or group of authors can clearly be associated with a web link, such as for weblogs, then they should be included in the reference.

Authors may wish to make use of reference management software to ensure that reference lists are correctly formatted.

Preparing tables

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When preparing tables, please follow the formatting instructions below.

- Tables should be numbered and cited in the text in sequence using Arabic numerals (i.e. Table 1, Table 2 etc.).
- Tables less than one A4 or Letter page in length can be placed in the appropriate location within the manuscript.
- Tables larger than one A4 or Letter page in length can be placed at the end of the document text file. Please cite and indicate where the table should appear at the relevant location in the text file so that the table can be added in the correct place during production.
- Larger datasets, or tables too wide for A4 or Letter landscape page can be uploaded as additional files. Please see [below] for more information.
- Tabular data provided as additional files can be uploaded as an Excel spreadsheet (.xls) or comma separated values (.csv). Please use the standard file extensions.
- Table titles (max 15 words) should be included above the table, and legends (max 300 words) should be included underneath the table.
- Tables should not be embedded as figures or spreadsheet files, but should be formatted using 'Table object' function in your word processing program.
- Color and shading may not be used. Parts of the table can be highlighted using superscript, numbering, lettering, symbols or bold text, the meaning of which should be explained in a table legend.
- Commas should not be used to indicate numerical values.

If you have any questions or are experiencing a problem with tables, please contact the customer service team at info@biomedcentral.com.

Preparing additional files

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As the length and quantity of data is not restricted for many article types, authors can provide datasets, tables, movies, or other information as additional files.

All Additional files will be published along with the accepted article. Do not include files such as patient consent forms, certificates of language editing, or revised versions of the main manuscript document with tracked changes. Such files, if requested, should be sent by email to the journal's editorial email address, quoting the manuscript reference number. Please do not send completed patient consent forms unless requested.

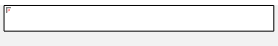
Results that would otherwise be indicated as "data not shown" should be included as additional files. Since many web links and URLs rapidly become broken, BioMed Central requires that supporting data are included as additional files, or deposited in a recognized repository. Please do not link to data on a personal/departmental website. Do not include any individual participant details. The maximum file size for additional files is 20 MB each, and files will be virus-scanned on submission. Each additional file should be cited in sequence within the main body of text.

If additional material is provided, please list the following information in a separate section of the manuscript text:

- File name (e.g. Additional file 1)
- File format including the correct file extension for example .pdf, .xls, .txt, .pptx (including name and a URL of an appropriate viewer if format is unusual)
- Title of data
- Description of data

Additional files should be named "Additional file 1" and so on and should be referenced explicitly by file name within the body of the article, e.g. 'An additional movie file shows this in more detail [see Additional file 1]'.

For further guidance on how to use Additional files or recommendations on how to present particular types of data or information, please see How to use additional files.



Centro de Epidemiologia Hospitalar

Tomei conhecimento. Nada a opor. À DC CSH.

02 de Junho de 2025

P/ A Diretora do Centro de Epidemiologia Hospitalar

(Prof.ª Doutora Ana Azevedo)

DIRECÇÃO CLÍNICA
2025 -06- 03

n.º 424 / 2024

SÃO JOÃO

PEDIDO DE AUTORIZAÇÃO

Realização de Investigação

Deliberado concordar, nos termos legais em vigor.

CONSELHO DE ADMINISTRAÇÃO DA ULS SÃO JOÃO, EPE - REUNIÃO DE
Presidente do Conselho de Administração
05 JUN. 2025

(Prof.ª Doutora Maria João Baptista)

Diretora Clínica para a área dos cuidados de saúde hospitalares	Diretora Clínica para a área dos cuidados de saúde primários	Enfermeiro Diretor	Vogal Executiva	Vogal Executivo
Dra. Elisabete Barbosa	Dra. Lígia Silva	Enf. Paulo Emílio Mota	Dra. Fernanda Oliveira	Dr. Vitor Leite

Exmo(a). Senhor(a) Presidente do Conselho de Administração do Centro Hospitalar Universitário de São João

Nome do Investigador Principal:
Rita Sofia Silva Nunes da Cruz Rato

Título da Investigação:
"Vascular Parkinsonism: Clinical and Imaging Patterns in Diagnostic Definition"

Centro Hospitalar São João
Centro de Epidemiologia Hospitalar
30 / 5 / 2025

Pretendendo realizar no(s) Serviço(s) de:
Neurologia e Neurorradiologia

a investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, autorização para a sua efetivação.

Para o efeito, anexo toda a documentação referida no dossier da Comissão de Ética do Centro Hospitalar Universitário de São João respeitante à investigação, à qual enderecei pedido de apreciação e parecer.

Com os melhores cumprimentos.

O Investigador/Promotor
Assinado por: **RITA SOFIA SILVA NUNES DA CRUZ RATO**
Num. de Identificação: BI14460823
Data: 2024.11.08 00:05:18 GMT Standard Time
assinatura
CHAVE MÓVEL

Porto, 08 *de* novembro *de* 2024 .

SÃO JOÃO | Encarregado de Proteção de Dados / Data Protection Officer
Entrada 08 / 11 / 2024

CES-IM005-2

ENCARREGADO DE PROTEÇÃO DE DADOS (EPD)
UNIDADE LOCAL DE SAÚDE SÃO JOÃO, E.P.E.

Paulo Alexandre Mota da Silva

Encarregado de Proteção de Dados da ULS SÃO JOÃO

epd@ulssjoao.min-saude.pt

Ref.ª CES ULSSJOAO: **424 / 2024**

Ref.ª EPD: **36 / 2025**

Título do Projeto

Vascular Parkinsonism: Clinical and Imaging Patterns in Diagnostic Definition

Responsável pelo tratamento	Rita Sofia Silva Nunes da Cruz Rato
Instituição	Unidade Local de Saúde de São João (ULS SÃO JOÃO)
	Faculdade de Medicina da Universidade do Porto (FMUP)
Investigador	**Interno** Externo
Contacto telefónico	912449797
Endereço Electrónico	u019135@ulssjoao.min-saude.pt
Profissional de Ligação	Não aplicável
Amostra	80 a 100

Análise de Risco: Tolerável | **Baixo** | Elevado | Muito Elevado

Parecer do EPD: 130/2025

Data: 21/05/2025

Finalidade: descrever e analisar os achados clínicos e imagiológicos de doentes seguidos em consulta de Neurologia de Doenças do Movimento por Parkinsonismo, com base na revisão dos seus processos clínicos. Iremos analisar a localização e extensão de doença cerebrovascular, definir doentes com parkinsonismo vascular "sensu strictu", caracterizar o contributo de doença vascular no fenótipo clínico e resposta a terapêutica implementada e ainda rever a possibilidade de se considerar outros diagnósticos alternativos.

Licitude: fundamento previsto no artigo **9(2)(j)**, com as garantias do **89(1)** do **RGPD**, e artigo **31(1)** da **LERGPD**.

Categorias de dados pessoais: variáveis identificadas com detalhe na AIPD, datada de 08/01/2025, **ponto 13**, tendo presente o **princípio da minimização dos dados.**

Conservação: os dados serão alvo de **pseudonimização**, armazenados em **local seguro**, em área restrita com acesso limitado ao Investigador Principal, com acesso a ficheiros protegido por **palavra-passe**, efetuando-se a conservação até a conclusão da investigação, durante o prazo máximo de **seis (6) meses**. Os dados recolhidos serão **eliminados / destruídos** após a finalização do estudo.

Comunicação de Dados: **há partilha** de dados pessoais (pseudonimizados).

Conclusão: Face ao exposto, e observadas as recomendações, entende-se que o presente projeto está em conformidade com o RGPD pelo que sou de **parecer favorável** quanto à sua realização.

Recomendações:

1. Reforçar as medidas de segurança previstas para a conservação dos documentos em formato de papel que impeçam o acesso à informação a pessoas não autorizadas, bem como o seu manuseamento indevido;
2. Garantir medidas de segurança adicionais no transporte dos dados com recurso a dispositivos electrónicos de armazenamento (Laptop, Pen, Cloud Institucional), nomeadamente através de medidas de cifragem e autenticação;
3. Garantir medidas de segurança adicionais (ex. transformar os dados com recursos a técnicas de generalização, perturbação e/ou como último recurso, a supressão de dados) para os dados que, ainda que pseudonimizados, contém elementos informativos que no seu conjunto possibilitam a re-identificação dos participantes, tendo presente a amostra em estudo (doentes seguidos em consulta de Neurologia de Doenças do Movimento por Parkinsonismo), em particular na fase de disseminação ou publicação dos resultados (incluindo repositórios científicos).
4. A chave de descodificação que permite a re-identificação dos titulares dos dados (doentes) deve ficar sempre na posse do Investigador Principal ULS SÃO JOÃO e protegida de acessos indevidos / terceiros;
5. Em caso de necessidade de extensão de prazo e/ou de qualquer alteração dos pressupostos atinentes ao presente parecer o Investigador Principal deverá solicitar a reapreciação do projeto de investigação junto do EPD.

Revisão AIPD:

☐ Data da próxima revisão:

☒ Não carece de revisão.

Anexos:

1. Processo CES n.º 424/2024
2. Parecer CES (20/12/2024)
3. AIPD (08/01/2025)
4. Protocolo de Investigação

Encarregado de Proteção de Dados
Assinado por: **PAULO ALEXANDRE MOTA DA SILVA**
Data: 2025.05.21 10:54:40+01'00'
Localização: ULS SÃO JOÃO

CARTÃO DE CIDADÃO

Parecer da Comissão de Ética do
Centro Hospitalar Universitário de São João
Unidade Local de Saúde de São João

Título do Projeto: Vascular Parkinsonism: Clinical and Imaging Patterns in Diagnostic Definition

Nome da Investigadora Principal: Dra. Rita Sofia Silva Nunes da Cruz Rato. Serão co-investigadores Natália Moreira Pacheco (estudante da FMUP) e o Prof. Doutor Rui Manuel Moreira Araújo (FMUP).

Onde decorre o Estudo: Nos Serviços de Neurologia e Neurorradiologia da ULS de São João. Apresentou declaração da Prof.ª Doutora Elsa Azevedo e do Dr. José Fonseca.

Objetivos do Estudo:
O objetivo deste estudo observacional retrospetivo é descrever e analisar os achados clínicos e imagiológicos de doentes seguidos em consulta de Neurologia de Doenças do Movimento por Parkinsonismo, com base na revisão dos seus processos clínicos.
Analisar a localização e extensão de doença cerebrovascular, definir doentes com "parkinsonismo vascular sensu strictu", caracterizar o contributo de doença vascular no fenótipo clinico e resposta a terapêutica implementada e ainda rever a possibilidade de se considerar outros diagnósticos alternativos.

Conceção e Pertinência do estudo:
O estudo é pertinente e adequado, porquanto consta no protocolo submetido à CE: "O parkinsonismo vascular combina sintomas de parkinsonismo com doença cerebrovascular. Alguns autores questionaram recentemente a existência do "parkinsonismo vascular" como uma entidade clínica distinta, pois os sintomas podem ser confundidos com outras condições vasculares. Os estudos de correlação entre sintomas clínicos e achados de imagem são limitados. A doença cerebrovascular é comum na população e pode ocorrer independentemente de processos neurodegenerativos primários. Com os avanços terapêuticos recentes nas doenças neurodegenerativas, como a introdução de novos medicamentos que visam vias metabólicas, como os agentes GLP-1, é crucial distinguir pacientes com parkinsonismo vascular "sensu strictu" de formas idiopáticas primárias".
Estudo observacional, retrospetivo, de doentes seguidos em consulta externa de Neurologia por Parkinsonismo, numa amostra estimada de 60 doentes.
Estão definidos os critérios de inclusão e as variáveis a ser recolhidas: idade, sexo, antecedentes (HTA, Tabagismo, DM, consumo etílico, IMC, sedentarismo, dislipedimia, SAOS, FA sedentarismo), estadio de parkinsonismo: Hoehn-Yahr e UPDRS, início de apresentação de sintomas (agudo, subagudo, crónico), idade de início dos sintomas, predomínio de sintomas Mis; alteração na marcha (quedas, freezing, base alargada, pequenos passos, festinação, balanceio dos braços durante a marcha, apraxia da marcha); tremor em repouso, rigidez em roda dentada, bradicinesia, sinais corticoespinhais, sinais cerebelosos, MMSE, alterações urinárias, cumprimento de critérios para outras doenças, tratamento médico, exames de imagem (RM,DATASCAN).

Benefício/risco:
Estudo observacional que utilizará dados clínicos previamente registrados.

Confidencialidade dos dados:

Os dados colhidos durante o estudo serão registados, em anonimato, numa base de dados, especificamente desenvolvida para o estudo. Os registos manter-se-ão confidenciais e anónimos de acordo com os regulamentos e leis aplicáveis. Cada doente será identificado por uma sequência de letras e números. Somente os investigadores terão acesso à descodificação desta sequência. No final do estudo, a chave de correspondência será eliminada. A confidencialidade será assegurada através do armazenamento dos dados numa base de dados guardada com palavra-passe, cujo acesso é apenas possível presencialmente através do acesso ao sistema informático pertencente à ULS São João.

Apresentou um pedido de reutilização de registos clínicos para Investigação e Desenvolvimento ao RAI, e uma 'avaliação sobre o impacto da proteção de dados' para o EPD.

Respeito pela liberdade e autonomia do sujeito de ensaio: Não aplicável

***Curriculum* da investigadora**: Adequado à investigação.

Data previsível da conclusão do estudo: maio de 2025

Conclusão: Proponho um parecer favorável à realização do estudo.

Porto, 20 de dezembro de 2024

Pedro Brito

O Relator da CE, Doutor Pedro Brito

Questionário eletrónico

n.º 424 / 2024

SÃO JOÃO

SUBMISSÃO DE PROJETO DE INVESTIGAÇÃO PARA PARECER E AUTORIZAÇÃO

Preenchimento em formato digital obrigatório

Caro/a Investigador/a

Este questionário vai ser objeto de apreciação pela Comissão de Ética (CE), que emitirá o competente parecer; pelo Responsável de Acesso à Informação (RAI), que emitirá um despacho de autorização ou indeferimento, relativamente à reutilização da informação a que pretende ter acesso; pelo Encarregado de Proteção de Dados (EPD), que emitirá um parecer, mediante a 'avaliação do impacto sobre a proteção de dados' (que deve anexar a este pedido); pelo Centro de Epidemiologia Hospitalar; sendo enviado, num último momento, para decisão institucional do Conselho de Administração do CHUSJ. Os respetivos despachos de parecer e autorização serão exarados no final deste documento, e enviados posteriormente, de modo a poder iniciar, nesse momento, a investigação a que se propõe.

IDENTIFICAÇÃO DO ESTUDO

Título do projeto:

"Vascular Parkinsonism: Clinical and Imaging Patterns in Diagnostic Definition"

Data prevista para início: 01 / 12 / 2024 Data prevista para o término: 01 / 05 / 2025

EQUIPA DE INVESTIGAÇÃO

1. Investigador principal

Nome: Rita Sofia Silva Nunes da Cruz Rato

Afiliação institucional: ☒ CHUSJ ☐ FMUP Outro: _____

Serviço/ Departamento: Neurologia

Grupo profissional: Médico (IFE) Cédula Profissional n.º: 74682

Contacto telefónico: 912449797 Endereço eletrónico institucional: rita.rato@ulssjoao.min-saude.pt

Formação em Boas Práticas Clínicas (GCP): ☐ Não ☒ Sim

2. Co-investigadores

Nome: Natália Moreira Pacheco

Afiliação institucional: Faculdade de Medicina da Universidade do Porto

Grupo profissional: Estudante Cédula Profissional n.º: _____

Contacto telefónico: 964476419 Endereço eletrónico institucional: up201905284@edu.med.up.pt

Nome: Rui Manuel Moreira Araújo

Afiliação institucional: ULS São João, FMUP

Grupo profissional: Médico Cédula Profissional n.º: 53368

Contacto telefónico: 917757675 Endereço eletrónico institucional: rui.araujo@ulssjoao.min-saude.pt

(acrescentar nº de investigadores, se apropriado ao projeto de investigação)

3. Promotor *(se aplicável)*: _____

CARACTERIZAÇÃO DA INVESTIGAÇÃO

1. Metodologia da investigação

☐ Qualitativa ☒ Mista (qualitativa+quantitativa) ☐ Outra. Qual? _____

Se quantitativa:

☐ Experimental ☒ Observacional ☒ Sem intervenção ☐ Com intervenção

Se experimental ou observacional com intervenção, qual o tipo de intervenção?

☐ Algoritmo de decisão diagnóstica/terapêutica ☐ Comunicação

☐ Outra. Qual? _____

2. Aleatorização dos braços de intervenção: ☐ Não ☐ Sim

3. Se observacional, qual o desenho?

☐ Coorte prospetivo ☒ Coorte retrospetivo ☐ Caso-controlo

☐ Transversal ☐ Ecológico ☒ Outro. Qual? Séries de casos

REALIZAÇÃO DA INVESTIGAÇÃO

Local onde se realiza a investigação: ☒ CHUSJ ☒ FMUP ☐ Outro

Serviço/ Departamento: Neurologia e Neurorradiologia

Existem outros Centros onde se realizará a investigação? ☒ Não ☐ Sim. Quais? _____

ENTIDADE(S) QUE TUTELA(M) A INVESTIGAÇÃO

1. CHUSJ – Serviço: Neurologia

2. FMUP – Departamento: Neurociências Clínicas e Saúde Mental

3. Outra instituição. Qual? _____

ORIENTADOR *(se aplicável)*

Nome: Prof. Rui Manuel Moreira Araújo

Afiliação: ULS São João, FMUP Endereço eletrónico institucional: rui.araujo@ulssaojoao.min-saude.pt

PROFISSIONAL DE LIGAÇÃO *(se aplicável - ver anexo)*

Nome: _____ Serviço: _____

ENQUADRAMENTO DA INVESTIGAÇÃO

Em trabalho académico? ☐ Não ☒ Sim Conferidor de grau? ☐ Não ☒ Sim

Síntese dos objetivos:

O objetivo deste estudo retrospetivo é descrever e analisar os achados clínicos e imagiológicos de doentes seguidos em consulta de Neurologia por Parkinsonismo, com base na revisão dos seus processos clínicos. Iremos analisar a localização e extensão de doença cerebrovascular, definir doentes com " parkinsonismo vascular sensu strictu", caracterizar o contributo de doença vascular no fenótipo clinico e resposta a terapêutica implementada e ainda rever a possibilidade de se considerar outros diagnósticos alternativos.

Fundamentação ética *(incluir informação sumária sobre o estado da arte, ganhos em conhecimento/inovação, ponderação geral sobre benefícios/risco)*:

O parkinsonismo vascular combina sintomas de parkinsonismo com doença cerebrovascular.Alguns autores questionaram recentemente a existência do "parkinsonismo vascular" como uma entidade clínica distinta, pois os sintomas podem ser confundidos com outras condições vasculares.Os estudos de correlação entre sintomas clínicos e achados de imagem são limitados. A doença cerebrovascular é comum na população e pode ocorrer independentemente de processos neurodegenerativos primários.Com os avanços terapêuticos recentes nas doenças neurodegenerativas, como a introdução de novos medicamentos que visam vias metabólicas, como os agentes GLP-1, é crucial distinguir pacientes com parkinsonismo vascular"sensu strictu"de formas idiopáticas primárias

PARTICIPANTES PREVISTOS PARA A INVESTIGAÇÃO

Estão definidos critérios de inclusão / de exclusão de doentes? ☐ Não ☒ Sim

Onde e como serão recrutados os participantes no estudo?

Pesquisa sistemática nos registos clínicos de doentes seguidos em consulta de Neurologia por Parkinsonismo

Qual é o tamanho amostral? Aproximadamente 60 participantes

Está prevista a recolha de material biológico específico para a investigação?

☒ Não ☐ Sim. Identifique e justifique:

BENEFÍCIO/RISCO DECORRENTE DA PARTICIPAÇÃO

Descreva os benefícios previsíveis:

Definir um padrão clínico e radiológico de Parkinsonismo Vascular que permitirá otimizar o diagnóstico e gestão da

Descreva os riscos/incómodos previsíveis:

Acesso aos registos clínicos dos doentes.

CONSENTIMENTO INFORMADO, ESCLARECIDO E LIVRE

Prevê a obtenção de consentimento informado? ☐ Sim ☒ Não

Se não, justifique: dado tratar-se de investigação com base na utilização de registos clínicos, sem intervenção, retr

Prevê informação escrita para os participantes? ☐ Sim. **Enviar modelo preenchido.**

☒ Não. Justifique: dado tratar-se de investigação com base na utilização de registos clínicos, sem intervenção, ret

O modelo para obtenção de consentimento é o modelo institucional do CHUSJ? ☐ Sim ☐ Não

PROTEÇÃO DE DADOS PESSOAIS

Necessita consultar registos clínicos? ☐ Não ☒ Sim

Está previsto o tratamento de dados pessoais? ☐ Não ☒ Sim

Se sim, de que forma é garantida a pseudonimização dos dados recolhidos? *(codificação, uso de filtros, siglas...)*

Os dados colhidos durante o estudo serão registados, em anonimato, numa base de dados, especificamente desenvolvida para o estudo. Os registos manter-se-ão confidenciais e anónimos de acordo com os regulamentos e leis aplicáveis. Cada doente será identificado por uma sequência de letras e números. Somente os investigadores terão acesso à decodificação desta sequência. No final do estudo, a chave de correspondência será eliminada. A confidencialidade será assegurada através do armazenamento dos dados numa base de dados guardada com palavra-passe, cujo acesso é apenas possível presencialmente através do acesso ao sistema informático pertencente à ULS São João.

Descreva o património informacional a que pretende ter acesso *(v.g.: nome, idade, data nascimento, idade, morada, diagnóstico, história clínica, tratamento...)*:

Idade, Sexo, antecedentes(HTA,Tabagismo,DM,consumo etílico,IMC,sedentarismo,dislipedimia,SAOS,FA sedentarismo),estadio de parkinsonismo: Hoehn-Yahr e UPDRS,inicio de apresentação de sintomas(agudo, subagudo, crónico),idade de início dos sintomas,predomínio de sintomas Mis;alteração na marcha(quedas, freezing, base alargada, pequenos passos, festinação, balanceio dos braços durante a marcha, apraxia da marcha); tremor em repouso, rigidez em roda dentada, bradicinesia, sinais corticoespinhais, sinais cerebelosos,MMSE,alterações urinárias,cumprimento de critérios para outras doenças, tratamento médico, exames de imagem (RM,DATASCAN)

Está prevista a criação de um Banco de Dados? ☒ Não ☐ Sim

Está previsto o registo de som ou de imagem dos participantes? ☒ Não ☐ Sim

O estudo envolve investigação genética? ☐ Não ☒ Sim

PROPRIEDADE INTELECTUAL

De quem será a propriedade intelectual da investigação e seus resultados?

☒ Investigador ☐ Promotor ☐ Serviço/CHUSJ ☐ Todos

DIVULGAÇÃO DOS RESULTADOS

Está prevista a divulgação dos resultados da investigação? ☐ Não ☒ Sim

Se sim, estão definidos critérios de publicação? ☒ Não ☐ Sim. Quais? _____

CONTRAPARTIDAS PARA OS PARTICIPANTES

Estão previstas contrapartidas para os participantes? ☒ Não ☐ Sim

Pela participação? ☒ Não ☐ Sim

Pelas deslocações? ☒ Não ☐ Sim

Pelas perdas salariais? ☒ Não ☐ Sim

Por outras perdas e/ou danos? ☒ Não ☐ Sim

EXAMES COMPLEMENTARES DE DIAGNÓSTICO

Estão previstos exames complementares de diagnóstico, para além dos inerentes à rotina assistencial?

☒ Não ☐ Sim. Quais? _____

Por quem serão suportados estes custos?

PROTOCOLO FINANCEIRO

Existe protocolo financeiro com o CHUSJ? ☒ Não ☐ Sim

SEGURO

Este estudo prevê intervenção clínica que implique a existência de um seguro para os participantes?

☒ Não ☐ Sim *(se sim, junte cópia da respetiva Apólice)*

Data previsível para fim do acesso aos dados: 01 / 05 / 2025

DOCUMENTOS ANEXOS *(em suporte digital)*

- [x] Pedido de autorização ao Presidente do Conselho de Administração do CHUSJ
- [x] Protocolo do estudo
- [ ] Caderno de recolha de dados (CRF)
- [x] Declaração Diretor(es) Serviço(s)
- [ ] Informação Orientador
- [ ] Profissional de ligação
- [ ] Informação aos participantes
- [ ] Modelo de consentimento a utilizar
- [ ] Instrumentos de avaliação *(escalas, inquéritos)* _____
- [x] Curriculum/a vitae *(investigador/es)*
- [x] Questionário para Encarregado de Proteção de Dados (EPD)
- [ ] Termo de Responsabilidade do Centro Académico Clínico *(para investigadores da FMUP que não pertençam ao CHUSJ)*
- [ ] Protocolo financeiro
- [ ] Outros: _____

TERMO DE RESPONSABILIDADE

Aceitação dos termos e condições de reutilização

Cumulativamente com as obrigações decorrentes da *Lei n.º 26/2016, de 22 de agosto*, maxime dos *n.º 2 e 3 do artigo 21 e o n.º 1 e 2 do artigo 12*, ao submeter o presente pedido, concordo e fico ainda juridicamente vinculado aos seguintes termos e condições:

- Comprometo-me a manter confidencial toda a informação à qual vou ter acesso;
- Após explicação do RAI do CHUSJ, embora a Lei 26/2016, de 22 de agosto, imponha como requisito a anonimização sem possibilidades de reversão, tal desiderato, é não só uma impossibilidade matemática já comprovada, como ainda resulta num prejuízo para a investigação, face à quantidade e à qualidade da informação a retirar à fonte, razão pela qual, concordando com o RAI, assumimos como compromisso a pseudonimização, o que impõe uma avaliação e gestão do risco, num quadro ético-jurídico que aceitamos e nos comprometemos a colaborar e respeitar;
- Não vou elaborar registos, suscetíveis de identificar ou tornar identificável a identidade das pessoas a quem os mesmos dizem respeito;
- Comprometo-me a consultar os processos clínicos nos termos e locais que me forem indicados para o efeito;
- Tomei conhecimento, que a violação de qualquer dos compromissos aqui assumidos, poderá resultar no apuramento de responsabilidades disciplinares, civis e penais, e ainda, à impossibilidade futura de aceder a informação de saúde para fins de investigação.
- Independentemente de requerer a Certidão de Reutilização, DAta REuse Certificate for Research (DARE), comprometo-me a citar as fontes, sempre que publicitar, no todo ou em parte, resultados da presente investigação.

COMPROMISSO DE HONRA E DECLARAÇÃO DE INTERESSES

Eu, Rita Sofia Silva Nunes da Cruz Rato ,

abaixo assinado, na qualidade de Investigador Principal, declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes na Declaração de Helsínquia (1960, e sucessivas emendas), da Organização Mundial de Saúde, da Convenção de Oviedo e das 'Boas Práticas Clínicas' (GCP/ICH) no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CE de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo, nos últimos três meses. Comprometo-me a entregar à CE o relatório final da investigação, assim que concluído.

Assinado por: **RITA SOFIA SILVA NUNES DA CRUZ RATO**
Num. de Identificação: BI14460823
Data: 2024.11.09 00.39.44 GMT Standard Time

Data: 09 / 11 / 2024

CHAVE MÓVEL

COMISSÃO DE ÉTICA CHUSJ/FMUP

Parecer da CE, emitido na reunião plenária de 20 / 12 / 2024

A Comissão de Ética para a Saúde APROVA por unanimidade o parecer do Relator, pelo que nada tem a opor à realização deste projecto de investigação.

-Centro Hosp. Univ. São João-
Comissão de Ética
Manuel Vaz Silva
Presidente

RAI 25000242

RAI - Responsável pelo Acesso à Informação no Centro Hospitalar Universitário de São João (Art. 9º, Lei 26/2016 de 22 de Agosto)

Gabinete de Apoio ao RAI
Recebido em 06/01/2025
A funcionária

SÃO JOÃO

AUTORIZADO
RAI - Responsável pelo Acesso à Informação no Centro Hospitalar de São João (Art. 9º, Lei 26/2016, de 22/8)
6/1/2025

CENTRO DE EPIDEMIOLOGIA HOSPITALAR

FACULDADE DE **MEDICINA**