



Clinical outcomes in elective total hip arthroplasty in Parkinson's disease: a systematic review of the literature

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- Parkinson's disease (PD) poses a significant challenge for the arthroplasty surgeon, owing to excessive muscle tone, higher fracture risk and poor bone quality. Several studies have reported high mortality, early failure and perioperative complications associated with hip fracture surgery in PD; however, no higher-level evidence exists regarding elective hip arthroplasty.
- The aim of our study was to perform a systematic review to evaluate the evidence basis and clinical outcomes pertaining to patients with underlying Parkinson's disease undergoing elective total hip arthroplasty (THA).
- We searched MEDLINE, EMBASE and The Cochrane Central Register of Controlled Trials to identify studies evaluating the safety and clinical outcomes of THA in patients suffering from Parkinson's. Our review conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.
- Ten studies encompassing 49,730 patients were included in our systematic review. Qualitative synthesis demonstrated comparable results between PD patients and controls with respect to one-year mortality and surgical site infections. PD patients experienced more medical complications, had a longer hospital stay and worse long-term implant survival. Some studies also reported a higher rate of dislocation, periprosthetic fractures and aseptic loosening.
- Decisions about the optimal articulation, the utilization of cemented components, dual-mobility cups or constrained liners were not uniform among included studies.
- THA in patients with Parkinson's disease can offer significant functional gains and pain relief. Surgical considerations pertain to the approach and ways to address instability, whereas emphasis should be placed on appropriate counselling and exploring whether potential improvement of life quality outweighs the risks.

Keywords: articulation; clinical outcomes; constrained liners; mortality rate; Parkinson's disease; surgical site infection; systematic review; total hip arthroplasty

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Introduction

Parkinson's disease (PD) is a neurodegenerative disorder characterized by the loss of dopaminergic neurons in the substantia nigra pars compacta in the midbrain.¹ The clinical manifestations can often be insidious and involve tremor, bradykinesia, rigidity contractures, dystonia and flexed posture.^{1,2} The burden of the disease has risen exponentially over the past decade and is estimated in 6.1 million individuals globally,³ with 1 million people suffering from the disease in the US alone.⁴

Spasticity, tremors and contracture result in abnormal muscle tone around the hip, and altered forces exerted on the hip joint.^{2,5} As a result, subluxation, degenerative diseases and secondary skeletal deformities are far more common.⁵ Postural instability predisposes Parkinson's individuals to sustain a fall, whereas reduced bone mineral density is the sequelae of vitamin D deficiency, physical impairment and immobilization induced hypercalcaemia.⁶⁻⁸ The fracture risk is also significantly higher in this patient cohort.⁹

PD poses a significant challenge for the orthopaedic surgeon for numerous reasons. Several studies have revealed a higher incidence of dislocation and aseptic loosening following hip replacement procedures, owing primarily to the excessive muscle tone.^{2,10-12} In addition to the disease influence on early failure of the prosthesis, higher fracture

risk and poorer bone quality has been suggested. Several studies have shown poor outcomes associated with hip fracture surgery in PD, namely high mortality, early failure and perioperative complications.^{5,13} Patients with PD and a fractured neck of femur experienced a higher reoperation and dislocation rate,¹³ whereas one study has notably reported a dislocation rate of 37% and a mortality rate of 47% six months following surgery.¹⁴ However, it would not be prudent to extrapolate conclusions drawn from a hip fracture or hemiarthroplasty surgery to the elective patient with PD, since there are differences in the severity of the procedure, the stage of the disease and the medical optimization of PD patients.

Clinical data on the optimal management and perioperative care in these patients are still scant. To the authors' best knowledge, there is no available systematic review providing higher-level evidence and guidance regarding the approach to this group. To this end, the aim of our study was to perform a systematic review to evaluate the evidence basis and clinical outcomes pertaining to patients with underlying Parkinson's disease undergoing elective total hip arthroplasty.

Methods

The study was registered with the PROSPERO database of systematic reviews (CRD42019121156) and was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹⁵

Search strategy

We conducted a systematic search of MEDLINE, EMBASE and The Cochrane Central Register of Controlled Trials (CENTRAL) from conception to June 2019. We utilized the NICE Healthcare Databases Advanced Search (HDAS) interface to perform our search.¹⁶ To identify registered ongoing trials, a search was performed on clinicaltrials.gov. We also hand-searched the reference lists of relevant reviews identified. We used the following search terms both as free-text items and in combination with Medical Subject Headings (MeSH): "Parkinson's", "total hip arthroplasty", "hip replacement".

Study selection and data extraction

Two investigators independently screened the titles and abstracts yielded by the search. The full manuscripts of potentially relevant studies were obtained, and data were independently extracted by two reviewers (KB, AF) based on a pre-piloted standardized data extraction sheet. Data were extracted on participants' characteristics, methodological features of the study, interventions, primary and secondary outcome events and results. Any discrepancies were resolved by consensus, after contacting a third investigator (ET) for the independent evaluation of the study.

Eligibility criteria and outcomes

Our inclusion criteria involved all studies reporting outcomes of a patient cohort suffering from Parkinson's disease who underwent elective total hip arthroplasty. Only studies published in English were included. Studies including patients with other neurological diseases were excluded. No restrictions were imposed in terms of publication date, publication status or the duration of follow-up. With respect to study design, we included randomized controlled trials (RCTs), cohort studies and case series. We excluded reviews, editorial comments, case reports and case series with ≤ 5 patients. A flow diagram illustrating the literature search according to the PRISMA statement¹⁷ is also provided (Fig. 1). The primary outcomes were mortality following elective total hip arthroplasty as well as implant survival and revision rate for any reason. Secondary outcomes included early (surgical site infection, pneumonia, urine infection, delirium, pulmonary embolism) and late complications (infection rate, loosening, dislocation and periprosthetic fractures), the implant of choice, surgical approach, length of stay and functional outcomes.

Methodological quality assessment

We utilized the Newcastle-Ottawa Scale (NOS)¹⁸ to evaluate the methodological rigour in cohort studies and case series. Discrepancies were resolved by consensus after contacting the senior author (ET). Risk of bias was assessed focusing on three areas of interest, namely the ascertainment of outcomes, the comparability of the cohorts and the selection of the group population.¹⁸

Results

A total of ten observational studies, encompassing 49,730 patients met the inclusion criteria for the systematic review and qualitative synthesis. Among these studies, three were retrospective case series and the remaining six retrospective cohort studies. Eight studies were conducted in Europe and two in the USA; follow-up ranged from 4 to 24 years. The mean age of patients was 73 years, and 49.8% were female in seven studies reporting gender. Further details on the study design, duration and participants' characteristics can be found in Table 1.

Owing to the small number of studies, the retrospective design and the large heterogeneity of the control groups we did not proceed to a quantitative synthesis of the data as it would be methodologically unsound. In addition, in three studies, the dataset did not permit extraction and adjudication of the outcomes in the elective group with PD alone.

Quality assessment and risk of bias in included studies

Outcomes were ascertained from medical records reviews except for Newman et al.¹⁹, Jansen et al.²⁰ and Meek

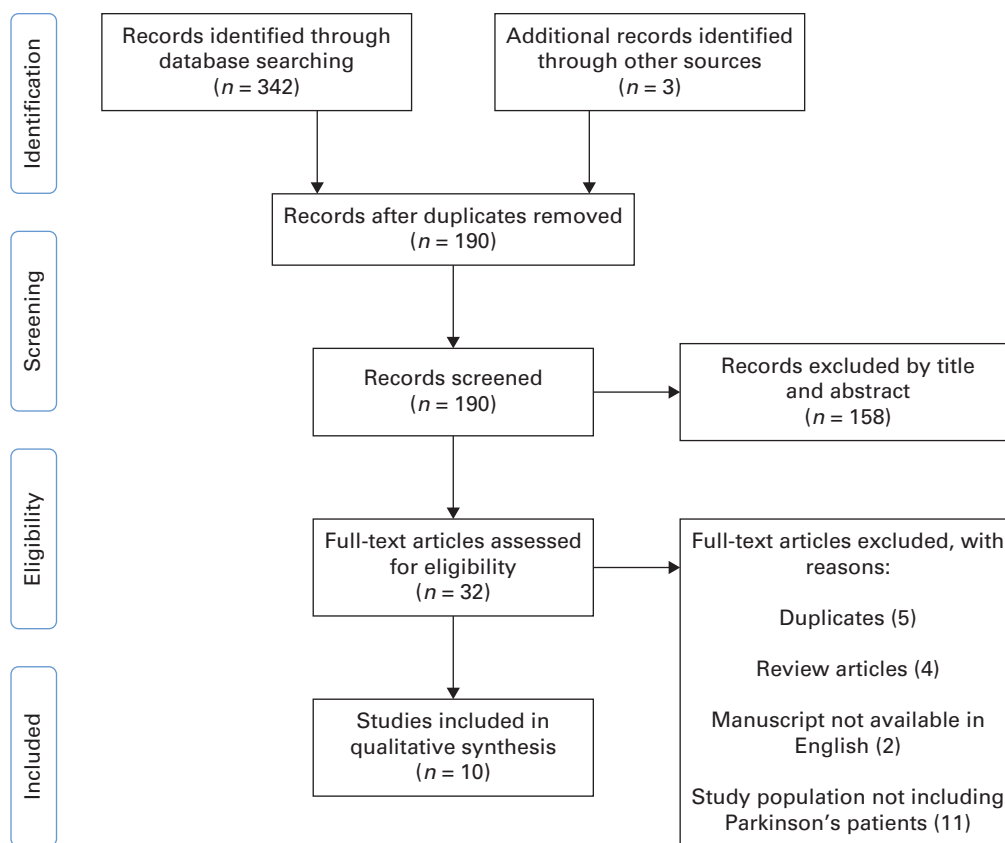


Fig. 1 Flow diagram depicting the phases of literature search.

et al²¹ where data were yielded from the interrogation of health registries. The overall quality level based on the Newcastle-Ottawa quality assessment was average; however, four studies were adjudicated with 9/9 stars for their methodological rigour (Table 2). Although outcome reporting among studies was inconsistent, most of them reported medical complications and the type of implant used, whereas mortality was reported by the authors in only five studies.

Mortality, surgical site infection and length of stay

Mortality and surgical site infection for all eligible studies reporting crude rate of events are presented in Tables 3 and 4. In the most recently published study, Wojtowicz et al²² reported no difference in mortality at 90 days and one year between PD and non-PD patients undergoing total hip arthroplasty (THA) (risk of death at 90 days, 0.62% vs. 0.61%, $p = 0.998$, and at one year 2.11% vs. 2.56%, $p = 0.670$). However, a significantly higher risk of death was noted in PD individuals nine years following the surgery compared to matched controls (54.35% vs. 28.05%, $p < 0.001$). Crude all-cause one-year mortality for both groups was also reported in Jämsen et al²⁰ with no significant differences observed among the groups (1.6% vs. 2.1%, $p = 0.396$). Lazennec et al²³ in their series

reported that 10/59 (16.9%) patients with PD undergoing THA had passed away by the end of their study for medical reasons not related to the surgery; perioperative mortality was reported by Weber et al²⁴ and occurred in 4/98 study subjects (4%), one patient died of a cerebrovascular accident, two of pneumonia and one of a massive pulmonary embolism.²⁴

The crude incidence of surgical site infection (SSI) was reported in seven studies^{19,20,23–27} and ranged from 0% to 7.7%. No significant differences were observed in the two largest studies, including nearly 45,000 patients. In a nationwide registry case-control study, Jämsen et al²⁰ reported an SSI incidence of 4.3% (37/857) in PD patients undergoing elective THA or TKR, whereas the respective incidence in the control group was 3.1% (80/2571), $p = 0.092$. In concordance, Newman et al¹⁹ reported no statistical difference in the occurrence of SSI among THA performed in patients with PD and matched controls ($p = 0.722$). Wojtowicz et al²² reported that 22% (95% CI, 11–40%) of the PD patients needing revision was due to a periprosthetic infection, whereas the respective percentage in the matched-control group was 2% (95% CI, 0–11%).

Finally, length of stay (LOS) was reported in two cohort studies, both of which suggested a longer stay for PD patients undergoing THA compared to matched controls;

Table 1. Participants' and studies' characteristics

Study	Study design	Groups	Mean follow up (years)	Time of Surgery	Preoperative disability	Mean age	Male number of patients (%)
Wojtowicz et al, 2019 ²²	RCC	Elective THA in PD patients with primary OA (N = 490)	4.7	1999–2012	EQ-5D 0.32 (p = 0.036), EQ-VAS 45.95 (p = 0.001), Pain VAS 65.81 (p = 0.046)	73	245 (50)
		Matched controls – Elective THA in non-PD patients with primary OA (N = 490)	5.6	1999–2012	EQ-5D 0.40, EQ-VAS 54.07, Pain VAS 62.44	73	245 (50)
Lazennec et al, 2018 ²³	RC	Elective THA in patients with PD (N = 59)	8.3	2002–2012	Hoehn and Yahr Stages: 1: 32.2%, 2: 40.7%, 3: 27.1%	72.5	N/R
Newman et al, 2018 ⁴	RCS	THA in patients with PD (N = 10,519)	N/R	2002–2013	Charlson/Deyo score 0: 58.68% 1: 25.26% 2: 16.06%	73	5,365 (51)
		THA in matched controls (N = 31,679)			Charlson/Deyo score 0: 64.43% 1: 24.30% 2: 11.27%	73	16,156 (51)
Weber et al, 2002 ²⁴	RCS	THA in patients with PD (N = 52 patients, 58 operations)	7.0	1970–1994	Hoehn and Yahr Stages: 1: 19.0%, 2: 69.0%, 3: 10.3%	N/R	N/R
		107 THA performed in 98 patients with PD (entire series population) for miscellaneous indications	7.1		Hoehn and Yahr Stages: 1: 13.1%, 2: 48.6%, 3: 35.5%, 4: 1.9%	72	49 (50)
Šponer et al, 2017 ²⁵	RCS	Elective THA in patients with PD (N = 10)	6.8	2005–2012	N/R	74	2 (20)
		THA in patients with PD for NOF fracture (N = 13)	4.5		N/R	76	6 (46.15)
Jämsen et al, 2014 ²⁰	RCS	857 with PD having elective THA or TKR (subset: 297 with PD undergoing THA)	5.4	1998–2009	N/R	72	347 (40.5)
		2571 matched controls undergone primary THR or TKR for OA during the study period not diagnosed with Alzheimer's or Parkinson's disease	5.5		N/R	73	1047 (40.7)
Mathew et al, 2013 ²⁷	RC	THA in patients with PD (N = 14 patients, 15 operations) – 10 for NOF fracture	3	2005–2009	Hoehn and Yahr Stages: 2: 60%, 3: 40%	76	6 (42.86)
Rondon et al, 2018 ²⁶	RCS	Elective THA in patients with PD (N = 52)	5.3	2000–2016	N/R	68.7	29 (55.4)
		Elective THA in 93 matched controls without PD			N/R	69.7	51 (55.1)
Sharma et al, 2018 ²⁸	RCS	Elective THA in patients with PD (N = 19)	N/R	2006–2016	N/R	N/R	N/R
		Elective TKR in patients with PD (N = 15)	N/R		N/R	N/R	N/R
		45 bipolar hemiarthroplasties for neck of femur fracture	N/R		N/R	78.3	19 (42.2)
Meek et al, 2006 ²¹	RC	Patients with PD undergoing THA, N = 2706	N/R	1998–2003	N/R	N/R	N/R

Notes. PD, Parkinson's disease; THA, total hip arthroplasty; NOF, neck of femur; TKR, total knee replacement; OA, osteoarthritis; RC, retrospective case series; RCS, retrospective cohort study; N/R: not reported, RCC: retrospective case-control; N, number of patients; EQ-5D, EuroQol- 5 Dimension; EQ VAS, EuroQol-visual analogue scales.

*Authors report that cells with a frequency between $n = 1$ and 11 were suppressed due to data use agreement.

Newman et al¹⁹ reported LOS 3.9 days vs. 3.6 days $p \leq 0.0001$ and Jämsen et al²⁰ 9 days vs. 7 days, $p < 0.001$.

Implant survival rates, revision rate and surgical complications

Revision rates, implant survival and surgical complications for all studies reporting crude rate of events are displayed in Table 3. Implant survival rates were reported at different time points among the included studies. Rondon et al²⁶ employed the longest follow-up; 10-year implant survivorship was significantly worse in PD patients compared to elective THA in matched controls ($p = 0.0024$). In concordance, Wojtowicz et al²² showed patients with PD were at higher risk of revision one year

(1.03% vs. 2.10%, $p = 0.256$) and nine years (5.44% vs. 1.75%, $p = 0.001$) after the primary procedure compared to matched controls. The five-year survival rate in the PD population was reported in two studies^{23,24} (79.7% and 93%).

With respect to other complications, although most of the included studies reported neutral results, Rondon et al²⁶ reported more patients in the PD group experienced dislocation, periprosthetic fracture and aseptic loosening. Jämsen et al²⁰ also demonstrated a higher dislocation rate in PD patients (6.1%) compared to matched controls in the first year but no difference in the rate of surgical site infections and revision. Wojtowicz et al²² presented data supporting the finding that dislocation and

Table 2. Newcastle-Ottawa Quality Assessment Scale

	Selection (max 4)				Comparability (max 2)		Outcome (max 3)			Total Score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest was not present at the start of study	Study controls for baseline characteristics	Study controls for any additional factors	Assessment of outcome	Follow up sufficient	Adequacy of follow up?	
Wojtowicz et al, 2019 ²²	*	*	*	*	*	*	*	*	*	9
Lazennec et al, 2018 ²³	*		*	*				*	*	5
Newman et al, 2018 ⁴	*	*	*	*	*	*	*	*	*	9
Weber et al, 2002	*		*	*			*	*		5
Šponer et al, 2017 ²⁵	*	*	*	*			*	*		6
Jämsen et al, 2014 ²⁰	*	*	*	*	*	*	*	*	*	9
Mathew et al, 2013 ²⁷	*		*	*			*	*	*	5
Meek et al, 2006 ²¹	*		*	*			*	*		5
Rondon et al, 2018	*	*	*	*	*	*	*	*	*	9
Sharma et al, 2018 ²⁸	*		*	*			*	*	*	6

aseptic loosening were more commonly reported indications for revision in PD patients than matched controls. Meek et al²¹ reported a very low incidence of dislocation in patients with PD ranging from 0% to 0.46% and failed to identify any correlation between PD diagnosis and dislocation rate.

Perioperative medical complications

Crude rate of events in all studies reporting the incidence of perioperative medical complications are summarized in Table 4. Urinary tract infection (UTI) was the most commonly reported medical complication in PD patients post-operatively, and its incidence varied from 0% to 4.8%. Newman et al¹⁹ presented the largest sample size in their nationwide database study encompassing approximately 10,519 patients with PD and 31,679 matched controls. They reported that patients with PD were more likely to experience delirium (2.16% vs. 0.24%, $p < 0.0001$) and UTI (4.8% vs. 3.58%, $p = 0.012$) perioperatively. One should also note the high prevalence of transfusion in the PD population, 2786/10519 (26.49%) versus 5841/31679 (18.44%), $p < 0.0001$. Šponer et al²⁵ and Sharma et al²⁸ reported a higher incidence of perioperative medical complications in the comparator group; notably though in both studies the control cohort comprised patients undergoing arthroplasty following a neck of femur (NOF) fracture.

Choice of implant and surgical approach

A wide variation in implant choice and surgical approach between studies was noted (Table 5). The most prevalent

surgical approach in all studies was the anterolateral.^{23–25,27} Less commonly, a transtrochanteric approach²⁴ was used, whereas other approaches included the posterolateral and direct lateral approaches.²⁴

The articulation of choice varied among the studies (Table 5), and authors reported the utilization of cemented and cementless components with success.^{20,23,25,27} In most studies, there was a tendency to opt for a cemented total hip replacement.^{20,25,27} A cementless dual-mobility bearing surface was also used by some authors to prevent instability.²³

Discussion

This systematic review synthesizes qualitative data pertaining to primary THA in patients with Parkinson’s disease. Our findings suggest that PD patients did not experience increased mortality in the immediate postoperative period compared to controls; however, long-term follow-up data showed a higher mortality risk, likely attributed to the disease progression. Patients with PD were at higher risk of revision for any reason following THA and developing postoperative medical complications, whereas there were insufficient data to support higher incidence of surgical site infection. A few studies also reported a higher risk of dislocation and periprosthetic fracture, nonetheless the evidence basis was insufficient to safely assume such a relationship. Furthermore, improved functional outcomes were noted in PD patients undergoing THA, whereas existing studies could not substantiate optimal implant and fixation.

Table 3. Surgical complications

Study	Groups	Revision rate	Implant survival	Dislocation	Periprosthetic fracture	Loosening	Surgical site infection	Other
Wojtowicz et al, 2019 ²²	Elective THA in PD patients with primary OA (N = 490)	Risk of revision 90-day (1.03%, p = 0.256), 1-year (2.10%, p = 0.021), 9-year 5.44%, p = 0.001		8% [§]	4% [§]	10% [§]	22% [§]	Technical failure 2% [§]
	Matched controls – Elective THA in non-PD patients with primary OA (N = 490)	Risk of revision 90-day (0.41%), 1-year (0.41%), 9-year (1.75%)		2% [§]	2% [§]	6% [§]	2% [§]	Technical failure 0% [§]
Lazennec et al, 2018 ²³	59/65 PD	Revision and reoperation rates: 8.5% at 2 years and 20.3% at 5 years		1 (1.7)	4 (6.8)	0	2 (3.3) – E. Coli	N/R
Newman et al, 2018 ⁴	10,519 PD	N/R	N/R	0 (0)	N/R	N/R	1 ≤ N ≤ 11* irrigation and debridement	Haematoma/seroma N = 165 (1.57)
	31,679 matched controls	N/R	N/R	0 (0)	N/R	N/R	38 (0.12) irrigation and debridement, p = 0.722	Haematoma/seroma N = 362 (1.14), p = 0.129
Weber et al, 2002 ²⁴	52/58 PD	Reoperation rate (5 years): 7%		0 (0)	0 (0)	1 (1.7)	0 (0)	N/R
	98/107 (entire series population)	Reoperation rate (5 years): 7%		6 (5.6)	1 (0.9)	1 (0.9)	1 (1)	N/R
Šponer et al, 2017 ²⁵	10 PD	N/R	N/R	1	1	N/R	0 (0)	N/R
	13 PD (THA for NOF fracture)	N/R	N/R	1	1	N/R	1 (7.7)	N/R
Jämsen et al, 2014 ²⁰	857 (elective THA or TKR, subset: 297 undergoing THA)	1-year and 3-year survival 98% and 96.8%		18 (6.1)	N/R	N/R	37 (4.3)	N/R
	2571 THR or TKR – matched controls	1-year and 3-year survival 98.6% and 96.3%		N/R	N/R	N/R	80 (3.1) p = 0.092	N/R
Mathew et al, 2013 ²⁷	14/15 PD	0 (0)	N/R	0 (0)	3 (21.4)	N/R	0 (0)	N/R
Rondon et al, 2018 ²⁶	52 PD	Higher rate of revision for PD, OR = 11.05 (95% CI 3.00–40.7, p = 0.0003)	Significantly worse, p = 0.0024	4 (7.7)	4 (7.7)	4 (7.7)	1 (1.9)	N/R
	93 matched controls		2-, 5- and 10-year survivorship 94.3%, 85.3%, 78.7%	0 (0) p = 0.0013	0 (0) p = 0.0013	2 (2.2)	0 (0)	N/R
Sharma et al, 2018 ²⁸	19 THA in PD patients	N/R	N/R	N/R	N/R	N/R	N/R	Broken K-wire 0 (0)
	15 TKR in PD patients	N/R	N/R	N/R	N/R	N/R	N/R	Broken K-wire 0 (0)
	45 bipolar hemiarthroplasties	N/R	N/R	N/R	N/R	N/R	N/R	Broken K-wire 1 (2.2)
Meek et al, 2006 ²¹	2706 PD	N/R	N/R	Annual dislocation rate 0–0.46%	N/R	N/R	N/R	N/R

Note. PD, Parkinson's disease; THA, total hip arthroplasty; NOF, neck of femur; TKR, total knee replacement; OA, osteoarthritis; HR, hazard ratio; N/R, not reported. Categorical data presented as number/sample size (percentage)

*Cells with frequency < 11 were suppressed owing to requirements in the data use agreement. [§]The percentage represents the indications for revisions not the percentage of complications.

Parkinson's disease is one of the most common neurological diseases an orthopaedic surgeon will have to address in individuals undergoing THA.²⁹ There are numerous published reports of suboptimal outcomes and increased perioperative mortality following surgical fixation of NOF fracture in the PD population.^{30,31} Notwithstanding, it is not prudent to extrapolate the results of hip fracture surgery in patients undergoing elective THA. Despite not being able to quantitatively synthesize data owing to significant heterogeneity, included studies did not unveil a higher mortality rate

for PD patients during the early postoperative period compared to controls. In the most recently published primary study, Wojtowicz et al²² suggested that THA did not result in an increased risk of death in the early postoperative period (90 days and one year), nevertheless PD patients experienced a higher long-term risk of death (nine years). Given Parkinson's disease is a progressive disorder affecting life expectancy, it is difficult to speculate what proportion of this risk could be attributed to the disease progression itself rather than the THA procedure.

Table 4. Medical complications

Study	Groups	Mortality	Pneumonia	UTI	Delirium/ cognitive impairment	PE	Other	Length of stay (days)
Wojtowicz et al, 2019 ²²	Elective THA in PD patients with primary OA (N = 490)	90-day (0.62%, p = 0.998), 1-year (2.11%, p = 0.670), 9-year 54.35%, p < 0.001	N/R	N/R	N/R	N/R	N/R	N/R
	Matched controls – elective THA in non-PD patients with primary OA (N = 490)	90-day (0.61%), 1-year 2.56%, 9-year 28.05%, p < 0.001	N/R	N/R	N/R	N/R	N/R	N/R
Lazennec et al, 2018 ²³	59/65 PD	10 (16.9)	3 (5)	2 (3.3)	12 (20.3)	N/R	Sacral pressure ulcers (2)	N/R
Newman et al, 2018 ⁴	10,519 PD	N/R	113 (1.07)	505 (4.80)	227 (2.16)	18 (0.17)	Transfusion: N = 2786 (26.49) MI: N = 100 (0.95)	3.9
	31,679 matched controls	N/R	229 (0.72), p = 0.113	1135 (3.58), p = 0.012	279 (0.88%), p < 0.0001	77 (0.24), p = 0.549	Transfusion: N = 5841 (18.44), p < 0.0001 MI: N = 446 (1.41), p = 0.109	3.6 p < 0.0001
Weber et al, 2002 ²⁴	52/58 PD	1 (1.9)	0 (0)	5 (9.6)	1 (1.9)	2 (3.8)	N/R	N/R
	98/107 (entire series population)	4 (4)	3 (3)	8 (8.1)	4 (4)	2 (2)	N/R	N/R
Šponer et al, 2017 ²⁵	10 PD	1 (10)	0 (0)	0 (0)	0 (0)	N/R	CVA 0 (0) Pressure sores 1 (10)	N/R
	13 PD (THA for NOF fracture)	1-year mortality: 4 (28.6)	4 (30.8)	9 (69.2)	2 (15.4)	N/R	CVA 1 (7.7) Pressure sores (15.4)	N/R
Jämsen et al, 2014 ²⁰	857 (elective THA or TKR, subset: 297 undergoing THA)	1-year mortality: 14 (1.6)	N/R	N/R	N/R	N/R	N/R	*9 (10)
	2571 THR or TKR – matched controls	1-year mortality: 54 (2.1)	N/R	N/R	N/R	N/R	N/R	*7 (6), p < 0.001
Mathew et al, 2013 ²⁷	14/15 PD	N/R	N/R	5 (35.8)	3 (21.4)	0 (0)	N/R	19
Rondon et al, 2018 ²⁶	52 PD	N/R	N/R	N/R	N/R	N/R	N/R	N/R
	93 matched controls	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Sharma et al, 2018 ²⁸	19 THA in PD patients	N/R	0 (0)	1 (5.3)	1 (5.3)	N/R	Anaemia 7 (37.0)	N/R
	15 TKR in PD patients	N/R	0 (0)	0 (0)	1 (6.7)	N/R	Anaemia 4 (26.7)	N/R
Meek et al, 2006 ²¹	45 bipolar hemiarthroplasties	N/R	6 (13.2)	9 (20)	1 (4.4)	N/R	Anaemia 10 (22.1)	N/R
	2706 PD	N/R	N/R	N/R	N/R	N/R	N/R	N/R

Notes. PD, Parkinson’s disease; THA, total hip arthroplasty; NOF, neck of femur; TKR, total knee replacement; OA, osteoarthritis; N/R, not reported; MI, myocardial infarction; CVA, cerebrovascular accident; UTI, urinary tract infection; PE: Pulmonary Embolism. Data presented as number/sample size (percentage). *Median (interquartile range).

As PD progresses patients may encounter rigidity, dystonia, bradykinesia, adiadochokinesia, contractures and tremor, hence increasing the theoretical risk of dislocation, periprosthetic fracture and implant failure. Notwithstanding, included studies reported conflicting findings in relation to surgical outcomes. Rondon et al²⁶ reported a higher incidence of dislocation and periprosthetic fracture in PD; in concordance, Wojtowicz et al²² identified PD participants were at higher risk of revision surgery, especially within one year following surgery, and also experienced more dislocations, corroborating the association of instability and PD. Notwithstanding, in their large registry-based analyses Meek et al²¹ reported a very low incidence of dislocations (annual dislocation rate 0–0.46%) and Newman et al¹⁹ reported no dislocations,

failing to demonstrate any significant correlation with Parkinson’s diagnosis. Jämsen et al in the Finnish registry data reported that 6.1% of PD patients sustained a dislocation; however, no difference was noted in the indication for revision between the two groups.²⁰ In order to make appropriate inferences though, one has to be considerate of the inherent limitations associated with registry data comprising data completeness, incorrect coding, missing data and selection bias. It is also noteworthy, that in most studies the dislocation incidence pertains to patients experiencing a dislocation and not the number of dislocations, failing to address the issue of recurrent instability. Surgical considerations to address the increased risk of instability include larger heads, dual-mobility implants or constrained liners.^{32,33} The option

Table 5. Type of implants and surgical approach used

Study	Patients/THA	Type of stem	Type of cup	Femoral head/ bearing couple	Approach
Wojtowicz et al, 2019 ²²	Elective THA in PD patients with primary OA (N = 490) Matched controls – Elective THA in non-PD patients with primary OA (N = 490)	Cemented 442 (90%), Uncemented hybrid 19 (4%)	23 (5%), Hybrid 6 (1%), Reverse hybrid 19 (4%)	N/R	N/R
Lazennec et al, 2018 ²³	59/65 PD	Primary THA: hydroxyapatite-coated, double-tapered titanium stem (N = 38), Modular global stem (N = 4). Revision THA: (optimum stem, N = 4).	Cementless acetabular implant	Primary and revision: dual-mobility bearing surface	Anterolateral (59)
Newman et al, 2018 ⁴	10,519 PD 31,679 matched controls	N/R N/R	N/R N/R	N/R N/R	N/R N/R
Weber et al, 2002 ²⁴	52/58 PD 98/107 (entire series population)	N/R 17 types of femoral component designs used, 103 were cemented	N/R 16 types of acetabular component designs used, 94 were cemented	N/R N/R	N/R Anterolateral (56) Transtrochanteric (36), Posterolateral (12), Direct lateral (3)
Šponer et al, 2017 ²⁵	10 PD 13 PD (THA for NOF fracture)	Cemented (9), Cementless (1) Cemented (12), Cementless (2)	Cemented (8), Cementless (2) Standard Acetabular liner (7) With elevated rim/lipped (3) Cemented (13), Cementless (1), Standard acetabular liner (8), With elevated rim/lipped (6)	28 mm (7) 32 mm (3) 28 mm (13) 32 mm (1)	Anterolateral Watson-Jones approach (10) Anterolateral Watson-Jones approach (14)
Jämsen et al, 2014 ²⁰	857 (elective THA or TKR, subset: 297 undergoing THA) 2571 THR or TKR – matched controls	Cemented (165), Resurfacing hip prosthesis or UKR (20) Cemented (449), Resurfacing hip prosthesis or UKR (90)	N/R N/R	N/R N/R	N/R N/R
Mathew et al, 2013 ²⁷	14/15 PD	Cemented: (13) Cementless: (2)	Cemented: (13) Uncemented: (1)	N/R	Primary THA: Anterolateral Watson-Jones approach (11), Revision: Bauer's approach (4)
Rondon et al, 2018 ²⁶	52 PD 93 matched controls	N/R N/R	N/R N/R	N/R N/R	N/R N/R
Sharma et al, 2018 ²⁸	19 THA in PD patients 15 TKR in PD patients 45 bipolar hemiarthroplasties	Cemented Müller straight stem (N = 7) Cementless CLS stem (N = 10), Cementless fitmore stem (N = 2) Innex Knee System (N = 6), PFC Sigma System (N = 7), Link rotation knee (N = 2) Cemented Bikontakt stems (N = 23) Cemented Müller straight stems (N = 22)	Standard Wagner cup (N = 2), Allofit cup (N = 16), Acetabular reinforcement ring (N = 1) N/R N/A	Polyethylene/ceramic bearing in all cases. Femoral head diameter: 32 mm in all cases. N/R N/A	N/R N/R N/R
Meek et al, 2006 ²¹	2706 PD	N/R	N/R	N/R	N/R

Notes. PD, Parkinson's disease; THA, total hip arthroplasty; NOF, neck of femur; TKR, total knee replacement; N/R, not reported; N/A, not applicable; OA, osteoarthritis; UKR, uni-compartmental knee replacement.

*Note that nine operations were carried out for NOF.

of cemented components should also be considered in osteoporotic individuals. In our systematic review, the articulation choice, the utilization of cemented components, dual-mobility cups or constrained liner was not uniform among studies. Lazennec et al²³ reported a low complication rate with dual-mobility bearing surface – only one patient sustained dislocation – and satisfactory long-term outcomes. A recently published study, with a seven-year mean follow-up, has also reported favourable long-term results in patients with constrained

liners during revision THA;³⁴ 80% of patients were free from instability at 10 years, however, worse acetabular survivorship was evident. The use of dual-mobility cups or constrained liners in selected cases, concerning low-demand individuals with a high risk of instability may be justifiable, although more long-term studies are needed to elucidate the downsides. In relation to the surgical technique, most surgeons utilized the anterolateral approach, followed by the transtrochanteric. Further to this, accelerated wear affecting the clinical longevity of

the implant was suggested, with studies reporting worse 5- and 10-year implant survivorship in the PD population.

There was a consensus among the two largest registry studies^{19,20} with regard to PD patients needing longer hospitalization. Furthermore, studies indicated that patients with PD experienced an increased risk of medical complications in the perioperative period, with UTI and delirium being more common. Hence, emphasis should be placed on facilitating early rehabilitation and preventing complications such as pneumonia, deep vein thrombosis (DVT) and UTI. As well as this, the input of and collaboration with a neurologist is advised, allowing optimization of the pharmacological treatment and aiming at normalizing the muscle tone.³⁵

Šponer et al,²⁵ Rondon et al²⁶ and Wojtowicz et al²² were the only three studies evaluating functional and pain outcomes. Wojtowicz et al²² found that one year following THA, PD patients had a diminished improvement in health and quality of life PROMS (patient-reported outcome measures), compared to the matched non-PD control group. Nonetheless, the improvement in these scores postoperatively was significant, indicating that THA may provide life-changing improvement of life quality and alleviation of pain in PD patients. Šponer et al reported patients with PD experienced good or excellent pain relief following THA,²⁵ whereas Rondon et al showed improved functional outcomes but not to the extent observed in patients without PD.²⁶

This systematic review does have limitations. First, the evidence base consists primarily of retrospective case series and cohort studies as well as national registry reviews, thus rendering evidence less robust and more prone to selection, reporting and interpretation bias. It should also be noted that four^{20,21,24,27} of the included studies were conducted more than ten years ago, limiting generalization of the results in the current clinical setting as treatment modalities for THA and PD have evolved. Second, we were not able to pool data and present cumulative incidence of adverse events and mortality, owing to the significant heterogeneity of the control groups. Third, most of the studies did not report PD severity and progression of the disease, potentially limiting our ability to extrapolate and draw conclusions for the PD patient population. Finally, even though the annual incidence of THA in Parkinson's patients has been reported at 5% to 8% in registry reviews,²¹ it remains relatively infrequent; therefore studies may be underpowered to unveil a difference in mortality and complications.

THA in patients with Parkinson's disease is a successful treatment that can offer significant functional gains and pain relief with a modest complication rate. Notwithstanding, this cohort of patients appears to have a higher risk of revision, medical complications and longer perioperative hospitalization. Appropriate counselling exploring whether potential improvement of life quality outweighs

the risks and managing patients' expectations are of utmost importance in this population. Based on the underlying evidence and the results of this systematic review, we are not able to advocate for any articulation, approach or type of fixation. The only primary study in our systematic review reporting the use of dual-mobility bearing surface,²³ showed satisfactory long-term outcomes suggesting potential benefits of dual-mobility in PD patients. Although not supported by the findings of this review owing to insufficient evidence, constrained or dual-mobility liners and large-diameter femoral heads may be used to decrease instability in selected PD patients.^{34,35}

Surmounting any challenges surrounding study design in patients with PD, more adequately powered, prospective studies are needed to evaluate long-term outcomes. Such studies could involve studying different articulations, approaches, and types of fixation in PD patients, matched for preoperative disability score, in order to enable clinically meaningful conclusions.

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