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Prevalence of Major Neurocognitive Disorder in Patients Admitted with Hip Fractures and the Associated Postoperative Delirium and Other Surgical Outcomes - A Prospective Cohort Study (Hippod Study)

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ABSTRACT

Introduction: *Major Neurocognitive disorder (NCD) and hip fractures are two serious problems in aging population. They are associated with morbidities including postoperative delirium (POD). We aimed to look at the prevalence of major NCD in hip fractures in our locality and their association with POD.*

Methods: *It was a prospective cohort study. Patients ≥ 65 years old with hip fractures communicable in Cantonese were included. They were screened with Hong Kong Montreal Cognitive Assessment 5-min protocol before operation. They were reviewed postoperatively with 3-Minute Diagnostic Interview for Confusion Assessment Method to assess the presence of POD. The primary outcome was the incidence of delirium between patients with or without preoperative major NCD. Secondary outcomes including surgical outcomes and length of hospital stay were investigated.*

Results: *The study was conducted between November 2020 and March 2021. One hundred ninety-two patients were screened, and 122 patients were included. Among the 192 patients screened, 97 (50.5%) were found to have major NCD. POD was found in 68.1% and 21.3% of patients with or without major NCD respectively. ($p<0.001$, odds ratio 4.857 (95% CI 2.046-11.531)). Total length of stay in hospital was longer when POD developed ($p<0.05$).*

Conclusion: *High prevalence of major NCD was found in geriatric hip fracture patients. Pre-existing major NCD was an independent risk factor in developing POD. Both major NCD and POD were prevalent but not sufficiently addressed in our locality. A multidisciplinary collaboration between anesthetists, geriatricians and allied health workers may help to prevent POD and reduce its severity.*

Keywords

Preoperative, Major NCD, Postoperative delirium, Hip Fracture.

Introduction

Geriatric hip fracture is a global problem in aging population. It is associated with morbidities and high mortality [1,2]. The consequences are to not only patients but also their caretakers and the healthcare system. Different societies were trying to tackle this problem over the last decades however the outcomes were inconsistent [3]. One of the major postoperative morbidities was postoperative delirium.

Postoperative delirium (POD) is a postoperative state in which patients have disturbance of consciousness accompanied by

impaired attention or ability to focus that cannot be explained by a pre-existing neurocognitive disorder. POD is associated with extended lengths of hospital stay, increased morbidities, and subsequent functional and cognitive decline [4,5]. Patients who have femoral neck fractures experience delirium three times more than patients undergoing non-orthopedic surgeries [6]. The incidence of POD in patients receiving surgeries for hip fractures varies between 9% to 65% from different studies due to the various criteria in defining delirium and heterogeneous clinical settings [7]. One local study demonstrated a 21.3% incidence of developing POD in orthopedic patients [8]. This figure included both patients with and without preoperative cognitive impairment. We expected the figures to be higher in the cognitive impaired group.

Patients with major NCD coming for hip surgeries might have more issues as with poorer capability in adapting to strange environment and tolerance to pain. The associated problems with major NCD will complicate the course of hospital stay and subsequent outcomes. The evidence for effective management and prevention of major NCD is still inadequate so far [9].

According to the figures quoted by the Legislative Council in 2017, prevalence of major NCD in Hong Kong was 5-8% among age over 65 [10]. We were expecting a severe under-reporting of this disease and it would be on the rise over the past few years. As with the shared risk factors for major NCD and hip fractures [11], the prevalence of major NCD in hip fracture patients was expected higher and was reported up to 75% [12-16].

In this study, we would like to survey the prevalence of major NCD in hip fracture patients in our locality and their associated surgical outcomes especially postoperative delirium comparing to patients without major NCD.

Methods

This was a prospective cohort study. Patients ≥ 65 years old admitted to Pamela Youde Nethersole Eastern Hospital (PYNEH) with hip fractures were screened with Hong Kong Montreal Cognitive Assessment 5-min protocol (HK-MoCA 5-min protocol). They were included if they were communicable in Cantonese and able to complete the HK-MoCA 5-min protocol.

The HKEC Research Ethics Committee approved the study. Informed consents were obtained from participants or their relatives according to their mental capacity. Due to COVID-19 pandemic during the study period, visiting was not allowed for non-critical patients. Verbal consents were obtained from the relatives over phone if the patient was not fit for consent. Written consents were obtained later in the relatives' convenience.

Participants were excluded if they were not surgical candidates or unable to complete HK-MoCA 5-mins or scored zero in this test. Patients would only be recruited for their first operation if they had repeated operations during the same admission.

HK-MoCA 5-min protocol was used to assess the presence of major NCD as soon as possible after admission. Patients were excluded if the screening tests were not done before surgical fixation. HK-MoCA 5-min protocol was selected for the preoperative screening because it was easy to learn and administer. It was also shown to have high validity and was equally reliable as the full version of MoCA in patient screening [17-20].

Participants were reviewed postoperatively with 3-Minute Diagnostic Interview for Confusion Assessment Method (3D-CAM) to assess the presence of POD on postoperative day 1 to day 3, or on the day of discharge from the acute admission ward whichever earlier. The assessments were done by occupational therapists, anesthetists or nursing staffs who have been trained to perform the assessments on patients.

3D-CAM was selected for assessing postoperative delirium in our study. A standardized evidence-based tool enables non-psychiatrically trained staff to identify delirium quickly and accurately in both clinical and research settings [21-24].

The primary outcome was the incidence of postoperative delirium in patients with or without preoperative major NCD. We also measured a set of secondary outcomes including 30-day mortality, respiratory complications, cardiovascular complications such as acute coronary syndrome, congestive heart failure, new onset arrhythmia, thromboembolic events, gastrointestinal bleeding, acute renal failure as with creatinine >20% of the baseline, ICU admission, cardiac arrest, postoperative day 30 inpatient rate, new institutionalization, length of stay in acute admission ward and total length of hospital stay.

Statistics

We estimated 40% of our geriatric hip fractures patients had major NCD [11-16]. With a hypothesis that patients with preoperative major NCD would experience twice the risk in developing POD, a sample size of 120 patients was required to provide a power of 80% with 95% confidence interval. 122 patients were decided to be recruited to prepare for potential loss of data during follow-up.

Chi-Square test and Fisher's exact test were used for categorical data. Mann-Whitney U test was used for continuous variables. All statistical analysis was done by SPSS Version 26. p-value <0.05 is considered significant.

In view of the bias associated with observational study, inverse propensity score weighting was used for data adjustment. Age, ASA classification, days of waiting before OT, mode of anesthesia and previous documented NCD were treated as potential confounders. Length of stay in acute ward and the presence of postoperative complications were also considered as factors potentially affecting the outcome. The predicted probability of each data was generated by performing binary logistic regression to each of the suspected confounders and factors affecting outcome. The weighting of each data set was then determined by using ATT (Average effect of the

treatment on the treated) method (See Appendix 1).

Results

The study was conducted between 15th November 2020 to 28th March 2021. One-Hundred-ninety-two patients were screened of which 122 patients fulfilled the criteria and were included. The study was suspended between 7th December to 31st December 2020 due to severe manpower dearth in COVID pandemic.

Among the 192 patients screened, 97 (50.5%) were found to have major NCD. Only 13 of them were previously documented with this diagnosis. Three patients with documented NCD were not detected by the HK-MoCA-5min protocol.

Twenty-nine patients were excluded with MoCA score zero to eliminate possible preoperative delirium. Eighteen patients were excluded as MoCA test could not be done prior to operation. Other 12 patients were excluded for no consent. Five patients were transferred out of PYNEH before surgery and 6 patients were excluded as operation was finally not done. No patient dropped out from the study after inclusion (Figure 1).

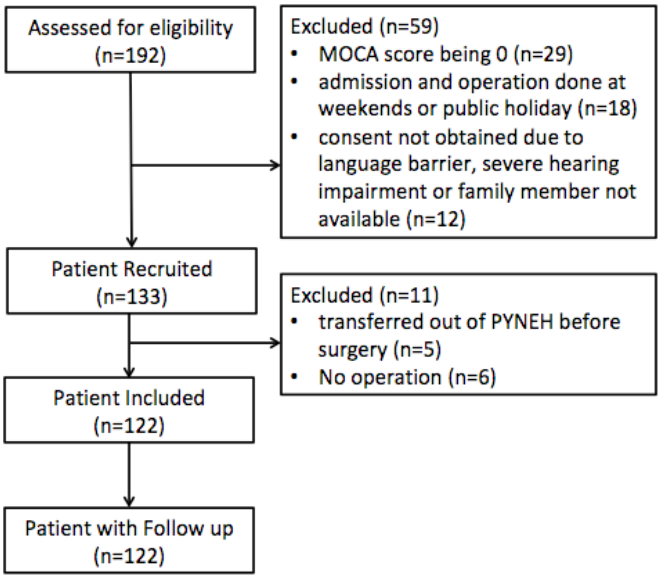

Figure 1: Flow chart of recruitment and follow up.

The mean age was 84.6 years old. Thirty-four (27.9%) patients were male and 88 (72.1%) were female. Major NCD was found in 48 (39.3%) patients while 74 (60.7%) patients were not. The baseline characteristics and demographics were shown in Table 1.

Forty-seven (38.5%) patients developed POD. Patients with pre-existing major NCD had a significant increased incidence of POD compared with patients without major NCD (32/47=68.1% vs 16/75=21.3%; p<0.001, See Table 2a).

Age and ASA classification were significantly correlated to preoperative NCD. In view of observational study subjected to bias from various confounding factors, inverse propensity score weighting was used for data adjustment to minimize bias caused by confounding factors.

After adjustment, we found that patients with pre-existing major NCD still had a significant increase in incidence of POD compared with patients without major NCD (32/48=66.7% vs 14/48=29.1%; p<0.001, Table 2b) with an odd ratio of 4.857 (95% CI 2.046-11.531).

Table 1: Baseline characteristics and demographics.

Age		82.7 (8.54)	87.6 (7.15)	0.004
Gender	Male	23 (31.1%)	11 (22.9%)	0.326
	Female	51 (68.92%)	37 (77.08%)	
ASA	2	33 (44.6%)	10 (20.8%)	0.007
	3	41 (56.41%)	38 (79.1%)	
MOA	GA	6 (8.11%)	1 (2.08%)	0.243
	SA	68 (91.9%)	47 (97.9%)	
Days to operation		2.24 (1.80)	2.40 (2.48)	0.866

Data are in n (%) or mean (SD).
ASA: American Society of Anesthesiologists Physical Status Classification, MOA: Mode of Anaesthesia, GA: General Anaesthesia, SA: Spinal Anaesthesia.

Table 2: The incidence of POD in patients with or without pre-existing major NCD**.**

(2a) Original		**Postoperative delirium**		
		No	**Yes**	**Total**
Pre-existing major NCD	No	59	16	75
	Yes	15	32	47
	Total	74	48	122

(2a) Original data showing a significant increase in incidence of POD in patients major NCD (16/75=21.3% vs 32/47=68.1%; p<0.001).

(2b) Adjusted		**Postoperative delirium**		
		No	**Yes**	**Total**
Pre-existing major NCD	No	34	14	48
	Yes	16	32	48
	Total	50	46	96

(2b) Adjusted data with inverse propensity score weighting with showing a significant increase in incidence of POD in patients with major NCD (14/48=29.1% vs 32/48=66.7%; p<0.001).

There was otherwise no significant difference in the secondary outcomes measured (Table 3).

These secondary outcomes were also compared between patients who developed POD and those did not. We found that the total length of hospital stay (LOS) was significantly longer in the group of patients who developed POD (29.95, 95% CI 26.69-33.2 vs 26.87, 95% CI 24.03-29.71; p<0.05). (Table 4).

Discussion

High prevalence of major NCD was found in our patients. This was 50.5% in the total screened patients and 39.3% in included patients. The high prevalence should draw the attention from the public and the authorities.

Table 3: Patients' outcome respective to the presence of Preoperative major NCD.

		Without Preoperative major NCD Original (Adjusted)	With Preoperative major NCD Original (Adjusted)	p value
LOS (acute ward)		10.91 (10.84)	10.17 (10.17)	0.280
LOS (total)		28.73 (28.61)	27.92 (27.92)	0.968
GI Bleeding	No	72 (45)	47 (47)	0.617
	Yes	2 (3)	1 (1)	
Thromboembolism	No	73 (46)	48 (48)	0.495
	Yes	1 (2)	0 (0)	
Acute Renal Failure	No	70 (44)	44 (44)	1.0
	Yes	4 (4)	4 (4)	
Respiratory Complications	No	65 (41)	43 (43)	0.759
	Yes	8 (7)	5 (5)	
Cardiovascular complications	No	71 (46)	44 (44)	0.677
	Yes	3 (2)	4 (4)	
ICU Admission	No	73 (47)	47 (47)	1.0
	Yes	1 (1)	1 (1)	
Cardiac Arrest	No	72 (48)	48 (48)	1.0
	Yes	2 (0)	(0)	
30-day Hospital Stay	No	53 (39)	35 (35)	0.331
	Yes	21 (9)	13 (13)	
30-day Mortality	Died	3 (2)	0 (0)	0.242
	Alive	70 (45)	48 (48)	
New Institutionalization	No	69 (42)	45 (45)	0.243
	Yes	5 (6)	3 (3)	
Overall Complications	No	59 (36)	39 (39)	0.459
	Yes	15 (12)	9 (9)	

Adjusted: Data adjusted with inverse propensity score weighting; LOS: Length of stay, ICU: Intensive Care Unit.

Table 4: Patients' Outcome respective to the Presence of POD.

		Without POD Original (Adjusted)	With POD Original (Adjusted)	p value
LOS (acute ward)		9.68 (10.30, 95% CI 7.62-12.89)	12.11 (10.79, 95% CI 8.22-13.36)	0.685
LOS (total)		27.12 (26.87, 95% CI 24.03-29.71)	30.43 (29.95, 95% CI 26.69-33.2)	<0.05*
GI Bleeding	No	73 (53)	46 (46)	0.378
	Yes	2 (3)	1 (1)	
Thromboembolism	No	74 (54)	47 (47)	0.293
	Yes	1 (2)	0 (0)	
Acute Renal Failure	No	68 (49)	46 (46)	0.085
	Yes	7 (6)	1 (1)	
Respiratory Complications	No	66 (49)	42 (42)	0.509
	Yes	8 (7)	5 (5)	
Cardiovascular complications	No	73 (54)	42 (42)	0.071
	Yes	2 (1)	5 (5)	
ICU Admission	No	73 (54)	47 (47)	0.293
	Yes	2 (2)	0 (0)	
Cardiac Arrest	No	73 (55)	47 (47)	1.0
	Yes	2 (0)	0 (0)	
30-day Hospital Stay	No	55 (45)	33 (34)	0.338
	Yes	20 (11)	14 (13)	
30-day Mortality	Died	2 (1)	1 (1)	0.706
	Alive	73 (54)	45 (45)	
New Institutionalization	No	69 (50)	45 (45)	0.288
	Yes	6 (5)	2 (2)	
Overall Complications	No	60 (44)	38 (39)	0.450
	Yes	15 (11)	9 (8)	

Adjusted: Data adjusted with inverse propensity score weighting, LOS: Length of stay, ICU: Intensive Care Unit.

The LOS was significantly longer in patients developed POD (29.95, vs 26.87; $p<0.05$) which was consistent with previous studies [28]. The reason for prolonged stay was not further investigated. We expected the functional status was largely compromised when POD was developed which affected their capability for discharge. Multiple workups might also be done to rule out organic causes of delirium which prolonged their stay. The overall pressure put to the healthcare system was increased with increased cost and resources.

Major NCD was found severely under-reported. Among the 97 patients identified with major NCD in our study, only 13 (13.4%) were previously documented to have similar findings. Most of our MoCA tests were done shortly after admission. We expected a minimal impact on the score by the hip fracture. We were not surprised by the under-reporting of this disease. The stigmatization and confusion with normal aging contributed to the major barriers in disease recognition. More resources should be allocated to ameliorate this deficit in our service.

POD was also under diagnosed. Studies reported that more than 50% of patients with delirium were undiagnosed [31,32]. POD was easily missed as delirium assessment has never been a parameter to measure routinely during postoperative period. Most of the medical staff are not familiarized with the techniques and components of delirium. It might be misdiagnosed as residual anaesthetic effects. We collaborated with occupational therapists in our study for cognitive assessment. However, after appropriate training and practices, any medical professionals could actually conduct CAM. Our nurses in operating theatre were able to carry out this assessment after a few weeks of training. We encourage the use of various assessment tools in detecting NCD and POD so to enhance early detection and management.

Pre-existing major NCD is an important risk factor for POD. This was not only shown in our study but also in previous literature [28]. This association was also found in non-surgical patients, which highlighted the independence and significance of major NCD to delirium in hospitalized patients. A recent study of non-surgical patients reported pre-existing major NCD as the main risk factor for delirium after hospitalization [29]. Previous studies revealed that delirium might be preventable in 30–40% of hospitalized elderly patients [33,34]. Identification of high-risk patients could be helpful in preventing POD. A comprehensive delirium prevention and intervention program could reduce the incidence and severity of delirium as well as shorten the duration of the episode. These include environmental control, reorientation, optimized oxygenation and hydration, infection control, early mobility, appropriate pain management, medication review, nutritional support, sleep hygiene, hearing and visual aids [35]. Before we are able to handle delirium effectively, it would be essential to initiate the routine assessment of cognitive function and confusion status. It would be a gorgeous movement to launch such in clinical practices but worth it to implement. We would like to suggest hospitals to form groups for cognitive and confusion screening preoperatively on geriatric hip fracture patients. Proactive geriatric or psychiatric consultation may decrease the risk of POD. Geriatricians, anesthetists and other involved healthcare professionals should work together as a multidisciplinary team for successful management of POD.

Three patients known to have major NCD preoperatively were not detected by HK-MoCA-5min protocol. Although both HK-MoCA and HK-MoCA 5-min protocol have very high sensitivity, specificity and correlation, there may still be discrepancies and inaccuracies. We did not have detailed information on their previous documented major NCD and the tests they received for diagnoses for those three patients.

There were several limitations in our study. Firstly, this was an observational study without randomization for patients with and without major NCD. Age and ASA score were found to be significantly associated with the presence of preoperative major NCD. Hence, inverse propensity score weighting was used for data adjustment to minimize the bias from confounding factors. The premorbid status was also not explored in detail. Therefore, other potential risk factors such as pre-existing cardiovascular or cerebrovascular events were not investigated for their contribution to POD and other secondary outcomes. Six patients were only assessed with 3D-CAM for 1 day postoperatively as they were discharged shortly after operation. This might underestimate the overall figure of POD. Moreover, this study was performed in a single institute, which might be subjected to selection bias. It would be more preferable if more hospitals would perform similar assessment for the risk factors contributing to POD. This would help in increasing awareness and training of various medical professionals in performing assessment tests in routine clinical practices.

Conclusion

High prevalence of major NCD was found in hip fracture patients up to 50.5%. Pre-existing major NCD was shown an independent risk factor for developing POD with an odd ratio of 4.857 (95%CI 2.046-11.531). Both major NCD and POD were commonly seen and were overlooked in our clinical settings. A multidisciplinary approach to identify patients with major NCD and those at risk for POD might help to prevent POD and reduce its severity.

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