Association between multidimensional prognostic index (MPI) and pre-operative delirium in older patients with hip fracture

Clarissa Musacchio1, Carlo Custodero2, Monica Razzano1, Rita Raiteri1, Andrea Delrio1, Domenico Torriglia1, Marco Stella3, Matteo Puntoni4,5, Carlo Sabbà2, Antonella Barone1 & Alberto Pilotto1,2*

Pre-operative delirium may cause delay in surgical intervention in older patients hospitalized for hip fracture. Also it has been associated with higher risk of post-surgical complications and worst functional outcomes. Aim of this retrospective cohort study was to evaluate whether the multidimensional prognostic index (MPI) at hospital admission was associated with pre-operative delirium in older individuals with hip fracture who are deemed to require surgical intervention. Consecutive older patients (≥ 65 years) with hip fracture underwent a comprehensive geriatric assessment to calculate the MPI at hospital admission. According to previously established cut-offs, MPI was expressed in three grades, i.e. MPI-1 (low-risk), MPI-2 (moderate-risk) and MPI-3 (high risk of mortality). Pre-operative delirium was assessed using the four 'A's Test. Out of 244 older patients who underwent surgery for hip fracture, 104 subjects (43%) received a diagnosis of delirium. Overall, the incidence of delirium before surgery was significantly higher in patients with more severe MPI score at admission. Higher MPI grade (MPI-3) was independently associated with higher risk of pre-operative delirium (OR 2.45, CI 1.21–4.96). Therefore, the MPI at hospital admission might help in early identification of older patients with hip fracture at risk for pre-operative delirium.

Delirium is a syndrome of acute change in cognition and alertness, often associated with psychotic behavior1. According to current estimates, delirium, with an incidence ranging from 14 to 56%, is one of the commonest complication in hospitalized older adults2 and is even more frequent in subjects undergoing urgent surgery3. Hip fracture represents the first cause of urgent surgery among older adults with over 300,000 hospital admissions each year in the United States4. In these patients, delirium usually occurs within the first 24–48 h after surgery with a frequency ranging between 20 and 50%5,6. However, most of the patients suffering from delirium already show it pre-operatively7. This may cause surgical delays which on turn increases delirium risk8–10. Pre-operative delirium is associated with worst prognosis compared to post-operative delirium including prolonged hospitalization, higher request of healthcare resources, loss of independence, institutionalization and death11–13. Nevertheless, systematic assessment is not yet universally applied and delirium is often underdiagnosed14. Considering the relevant health impact of delirium6, and the growing number of older adults undergoing falls with hip fracture4, there is a need of instruments able to early identify subjects more at risk to develop delirium since the pre-operative phases. This could help to design strategies for earlier and more appropriate intervention. It is becoming clear that multidimensional impairment of older patients may influence the clinical outcome of acute diseases15. It is also evident that etiology of delirium is likely multifactorial and linked to many other

1Department of Geriatric Care, OrthoGeriatrics and Rehabilitation, Frailty Area, E.O. Galliera Hospital, Via Mura delle Cappucine 16, 35121 Genoa, Italy. 2Department of Interdisciplinary Medicine, Clinica Medica e Geriatria "Cesare Frugoni", University of Bari Aldo Moro, Bari, Italy. 3Orthopedic Unit, Department of Geriatric Care, OrthoGeriatrics and Rehabilitation, Frailty Area, E.O. Galliera Hospital, Genoa, Italy. 4Clinical Trial Unit, Scientific Directorate, E.O. Galliera Hospital, Genoa, Italy. 5Clinical and Epidemiological Research Unit, University Hospital of Parma, Parma, Italy. *email: alberto.pilotto@galliera.it
geriatric syndromes (e.g. falls, functional decline, frailty, dementia). Recently, it has been shown that the multidimensional prognostic index (MPI), a predictive tool of mortality, based on a standardized comprehensive geriatric assessment (CGA), is an independent predictor of 6-month mortality in older patients with hip fracture.

The aim of the present study was to evaluate the usefulness of the MPI for prompt detection of older patients admitted to the hospital for hip fracture surgery and who were at risk for pre-operative delirium.

Methods

Study population. We conducted a retrospective observational cohort study on consecutive patients aged 65 years and older admitted from January 2017 to December 2017 to the Orthogeriatrics Unit of Galliera Hospital of Genoa, Genoa, Italy. Inclusion criteria were: (a) age ≥ 65 years, (b) diagnosis of hip fracture, (c) complete CGA at admission, (d) assessment of delirium during hospitalization, and (e) ability to provide an informed consent or availability of a proxy for informed consent. There were no specific exclusion criteria. Patients’ flowchart is presented in Fig. 1. Information on waiting time for surgery, type of anesthesia (i.e. general, spinal anesthesia alone or with peripheral nerve block, other types), presence of infections or anemia after surgery, and length of hospitalization were recorded.

Informed consent was obtained from all participants and/or their legal guardians. This study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines and adhered to the tenets of the World Medical Association’s Declaration of Helsinki.

The multidimensional prognostic index. The multidimensional prognostic index (MPI) is a well-validated tool measuring multidimensional frailty. At baseline the MPI was calculated from the data derived from a standard CGA which included information on the following eight domains: functional status evaluated with the activity of daily living (ADL) scale and the instrumental ADL (IADL) scale; cognitive status evaluated by the Short Portable Mental Status Questionnaire (SPMSQ); nutritional status evaluated by the Mini Nutritional Assessment-Short Form (MNA-SF); risk of developing pressure sores evaluated by the Exton Smith Scale (ESS); co-morbidity was examined using the Cumulative Illness Rating Scale (CIRS); number of drugs assumed by patients at admission and the co-habitation status (i.e. alone, in family or in institute) were also recorded. According to previous established cut-off, MPI was expressed in three grades, i.e. MPI-1 (low-risk MPI value ≤ 0.33), MPI-2 (moderate-risk MPI value between 0.34 and 0.66) and MPI-3 (high risk of mortality MPI value > 0.66).

Diagnosis of delirium. Screening of delirium was made before surgery using the four ‘A’ s Test (4AT). The 4AT is a composite test which assigns a score to the four following components: (a) alertness (0: fully alert or mild sleepiness for < 10 s after waking; 4: abnormal), (b) the Abbreviated Mental Test-4 for recall of age, date of birth, place (name of the hospital) and current year (0: no mistakes; 1: one mistake; 2: two or more mistakes or untestable), (c) attention assessed asking the patient to list months backwards starting from December (0: reciting ≥ 7 months correctly; 1: starts but recites < 7 months or refuses to start; 2: untestable), (d) acute change or fluctuating course in mental status within the last 2 weeks and persisting in the last 24 h (0: no; 4: yes). Summing the scores of the four components, we obtain a total score ranging from 0 to 12 with 0 indicating low probability to have delirium or severe cognitive impairment; 1–3: possible cognitive impairment and does not exclude the possibility of delirium; 4 or more suggesting possible delirium with or without cognitive impairment. Diagnosis of delirium was met whether the suspect based on 4AT score was confirmed by criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V).
define nominal statistical significance.

Statistical analysis. Descriptive statistics were used for continuous factors and expressed as mean and standard deviation or median and interquartile range (IQR). In case of categorical factors, absolute and relative frequencies (%) were reported. Fisher’s exact test was used to compare categorical factors. Normality of data was tested graphically (histograms and quantile–quantile plot) and through formal test (Shapiro–Wilk W test); independent sample t-test (in case of normally distributed data) or Mann–Whitney test (in case of not normally distributed data) were used for comparison of continuous variables between subjects with and without diagnosis of delirium. Logistic regression modelling was adopted to calculate odds ratios (ORs) and Wald test to estimate
distributed data) were used for comparison of continuous variables between subjects with and without diagnosis of delirium. Logistic regression modelling was adopted to calculate odds ratios (ORs) and Wald test to estimate

delirium. Patients with delirium were significantly older (87 ± 6.2 vs. 83 ± 6.8, p < 0.001), with a similar proportion of females (85.6% vs. 83.2%, p = ns) compared to patients without delirium. Length of stay was about 3 days longer in patients with delirium [11 (IQR, 8–15) vs. 8 (IQR, 6–11), p = 0.04], as well as post-

Ethical approval and informed consent. The study received formal ethical approval by the Ethical Committee of Regione Liguria, Italy. All participants gave written informed consent.

Results

Table 1. Characteristics of patients by presence of pre-operative delirium. IQR interquartile range, SD standard deviation. *p Value for t test (age), Mann–Whitney test (length of stay and time to surgery) or Fisher exact test.

| | Delirium (n=104) | No delirium (n=140) | Overall (n=244) | p Value*
|---|---|---|---|---
| Age, years, mean (SD) | 87 (6.2) | 83 (6.8) | 85 (6.9) | < 0.001
| Sex, n (%) | | | | 0.6
| Male | 15 (14.4) | 24 (17.1) | 39 (16.0) | |
| Female | 89 (85.6) | 116 (82.8) | 205 (84.0) | |
| Length of stay, days, median (IQR) | 11 (8–15) | 8 (6–11) | 9 (7–13) | < 0.001
| Time to surgery, days, median (IQR) | 3.5 (2–5) | 3 (2–4) | 3 (2–4) | 0.01
| Type of anesthesia, n (%) | | | | 0.04
| Spinal | 51 (49.0) | 56 (40.0) | 107 (43.9) | |
| Spinal + nerve block | 46 (44.2) | 61 (43.6) | 107 (43.9) | |
| General | 3 (2.9) | 3 (2.1) | 6 (2.5) | |
| Other | 4 (3.9) | 20 (14.3) | 24 (9.8) | |
| Post-operative anemia, n (%) | 84 (80.8) | 85 (60.7) | 169 (69.3) | 0.001
| Post-operative infection, n (%) | 61 (58.7) | 48 (34.3) | 109 (44.7) | < 0.001

Overall, 244 older adults with a diagnosis of hip fracture were eligible for the study. Patients were mainly female (84.2%) with a mean age of 85 (6.9) years, ranging from 65 to 102 years old. Before surgery, delirium occurs

In a multivariate logistic model adjusted for potential pre-, intra-, and post-operative confounders including gender, age, social support network, number of drugs, waiting time for surgery, type of anesthesia, and presence of infection or anemia after surgery, high-risk MPI category (MPI-3) at admission was independently associated with higher risk of pre-operative delirium compared to subjects in intermediate risk category (MPI-2) [OR 2.45, confidence interval (CI) 1.21–4.96, p = 0.01] (Table 3).

Statistical analysis. Descriptive statistics were used for continuous factors and expressed as mean and

Ethical approval and informed consent. The study received formal ethical approval by the Ethical Committee of Regione Liguria, Italy. All participants gave written informed consent.

Results

Table 1. Characteristics of patients by presence of pre-operative delirium. IQR interquartile range, SD standard deviation. *p Value for t test (age), Mann–Whitney test (length of stay and time to surgery) or Fisher exact test.

| | Delirium (n=104) | No delirium (n=140) | Overall (n=244) | p Value*
|---|---|---|---|---
| Age, years, mean (SD) | 87 (6.2) | 83 (6.8) | 85 (6.9) | < 0.001
| Sex, n (%) | | | | 0.6
| Male | 15 (14.4) | 24 (17.1) | 39 (16.0) | |
| Female | 89 (85.6) | 116 (82.8) | 205 (84.0) | |
| Length of stay, days, median (IQR) | 11 (8–15) | 8 (6–11) | 9 (7–13) | < 0.001
| Time to surgery, days, median (IQR) | 3.5 (2–5) | 3 (2–4) | 3 (2–4) | 0.01
| Type of anesthesia, n (%) | | | | 0.04
| Spinal | 51 (49.0) | 56 (40.0) | 107 (43.9) | |
| Spinal + nerve block | 46 (44.2) | 61 (43.6) | 107 (43.9) | |
| General | 3 (2.9) | 3 (2.1) | 6 (2.5) | |
| Other | 4 (3.9) | 20 (14.3) | 24 (9.8) | |
| Post-operative anemia, n (%) | 84 (80.8) | 85 (60.7) | 169 (69.3) | 0.001
| Post-operative infection, n (%) | 61 (58.7) | 48 (34.3) | 109 (44.7) | < 0.001

Overall, 244 older adults with a diagnosis of hip fracture were eligible for the study. Patients were mainly female (84.2%) with a mean age of 85 (6.9) years, ranging from 65 to 102 years old. Before surgery, delirium occurs

In a multivariate logistic model adjusted for potential pre-, intra-, and post-operative confounders including gender, age, social support network, number of drugs, waiting time for surgery, type of anesthesia, and presence of infection or anemia after surgery, high-risk MPI category (MPI-3) at admission was independently associated with higher risk of pre-operative delirium compared to subjects in intermediate risk category (MPI-2) [OR 2.45, confidence interval (CI) 1.21–4.96, p = 0.01] (Table 3).
Discussion
In the present study, we demonstrated that just from a standard CGA it is possible to obtain useful information to identify subjects at risk for delirium. Specifically, high-risk MPI category was associated with occurrence of pre-operative delirium among older adults undergoing surgery for hip fracture. Seniors with hip fracture are very vulnerable subjects at elevated risk of mortality. Indeed, in our cohort, we did not find any patient in MPI-1, the low mortality risk category. Multidimensional impairment before surgery could also identify subjects more prone to develop life-threatening complications as pre-operative delirium.

Table 2. MPI score and other subdomains according to diagnosis of delirium. Mean values of Exton Smith Scale are not available; * p value for Mann–Whitney test or Fisher exact test. IQR interquartile range, ADL activities of daily living, CIRS cumulative illness rating scale, IADL instrumental activities of daily living, IQR interquartile range, MNA-SF mini nutritional assessment short form, MPI multidimensional prognostic index, SD standard deviation, SPMSQ short portable mental status questionnaire.

| Factor                  | Delirium   | No delirium | p Value* |
|-------------------------|------------|-------------|----------|
| MPI classes, n (%)      |            |             |          |
| 2                       | 28 (26.9)  | 73 (52.1)   | <0.001   |
| 3                       | 76 (73.1)  | 67 (47.9)   |          |
| MPI, median (IQR)       | 0.75 (0.63–0.81) | 0.63 (0.56–0.75) | <0.001 |
| ADL, median (IQR)       | 0 (0–1)    | 1 (0–1)     | 0.1      |
| IADL, median (IQR)      | 1 (0–2)    | 2 (1–4.5)   | <0.001   |
| CIRS, median (IQR)      | 4 (2.5–5)  | 4 (2–5)     | 0.8      |
| SPMSQ, median (IQR)     | 4 (0–8)    | 9 (6–10)    | <0.001   |
| MNA-SF, median (IQR)    | 8 (5–10)   | 9 (7–11)    | 0.004    |
| Drugs, median (IQR), range | 5 (3–7), 0–14 | 5 (3–7), 0–13 | 0.3      |
| Co-habitation, n (%)    |            |             |          |
| Living with family      | 45 (43.2)  | 65 (46.4)   |          |
| Institute               | 19 (18.2)  | 14 (10.0)   |          |
| Living alone            | 40 (38.5)  | 61 (43.6)   |          |

Table 3. Multivariate logistic model for the diagnosis of pre-operative delirium. Odds ratios are also adjusted for gender, waiting time for surgery and number of drugs. CI confidence interval.
Incidence of pre-operative delirium in our cohort was 43% which is similar to previously reported estimates in older adults with hip fracture. In particular subjects with higher MPI score (MPI-3) at admission had 2.4 times higher risk to develop delirium before surgery, independently by other potential confounders.

The mechanisms underlying pre-operative delirium are still unclear. They might be partially different also from those of post-operative delirium, and mainly related to fracture-associated pain and adverse effects of analgesic treatments. A number of risk factors favoring delirium occurrence have been recognized and can be distinguished between predisposing and precipitating factors. Here, we found that elderly subjects who experienced pre-operative delirium were significantly older, and already more compromised at admission, having lower cognitive performance, poorer functional status and being more malnourished compared to those patients who did not have delirium. Post-operative complications as infections and anemia were associated with presence of delirium before surgery. Overall post-operative complications could explain also the longer length of in-hospital stay in the delirium group. In a recent meta-analysis, Smith et al. revised 32 studies for a total of 6704 included older adults with hip fracture. They assessed potential pre-, intra-, and post-operative risk factors for delirium. Consistently with our findings, they demonstrated that people with delirium are roughly three years older, more often institutionalized prior the hospital admission, and have lower cognitive scores as assessed by Mini Mental State Examination (MMSE). Presence of dementia at admission and higher American Society for Anesthesiologists (ASA) score (i.e. grade III and IV) are associated with six- and two-time higher risk of delirium, respectively. Other reports from older adults with hip fracture showed that risk factors for pre-operative delirium are partially different from those of post-operative delirium. Specifically, waiting time to surgery, number of comorbidities, use of opioids and benzodiazepines, and fever were associated with pre- but not post-operative delirium.

Our study demonstrated that pre-surgical multidimensional assessment using the MPI, a prognostic index based on data available from a standard CGA, was associated with occurrence of delirium independently by age and other potential confounders intervening later during hospitalization (e.g. delay of surgery, type of anesthesia, infections, anemia). Several prediction models have been proposed to identify in-patient older adults at risk for delirium, but few instruments have been validated specifically for detection of patients more prone to develop pre-operative delirium. In particular, the delirium elderly at risk (DEAR) tool, has been developed to predict incidence of delirium before surgery among older adults with hip fracture. It is a five-item scale assessing cognitive deficits, sensory impairment, functional dependence, substance use, and age (> 80 years old), with a score ranging from 0 (no risk factor) to 5 (all risk factors). However, the DEAR tool, using a cut-off value of 3, showed good specificity (82%), but quite low sensitivity (63%) in predicting pre-operative delirium. Collectively these data support the concept that multidimensional aggregate information, readily available in clinical practice and easy to obtain, could help physicians to predict occurrence of pre-operative delirium in older patients with hip fracture.

The present study has also some limitations. Firstly, since the study population included selected patients, it is possible that the sample is unrepresentative of older population hospitalized with hip fracture. Secondly, the retrospective design did not allow to systematically collect further information for example about: type of fracture, mechanism of injury, ASA score, delirium motor subtypes (hyperactive, hypoactive, mixed), analgesic and sedative treatments, or other potential post-operative complications. Finally, the study population was relatively small, and the patients were recruited from a single hospital. Therefore, larger prospective multicenter studies are needed to confirm and validate these findings.

In conclusion, the care of hospitalized older adults with hip fracture, who are at risk for delirium, requires a collaborative multidisciplinary effort involving geriatricians, orthopedic surgeons, anesthesiologists, and nurses. The CGA-based MPI, collected at hospital admission, might be a sensitive tool to early identify subjects at risk to develop pre-operative delirium and thus could represent a crucial step toward individualized decision making.

Data availability
The dataset is available from the corresponding author on reasonable request.

Code availability
All analyses were conducted using STATA software, and the code is available on request.

Received: 9 November 2021; Accepted: 19 September 2022
Published online: 08 October 2022

References
1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.). Am. Psychiatric Assoc. 21, 591–643 (2013).
2. Fong, T. G., Talebaev, S. R. & Inouye, S. K. Delirium in elderly adults: Diagnosis, prevention and treatment. Nat. Rev. Neurol. 5, 210–220. https://doi.org/10.1038/nrneurol.2009.24 (2009).
3. Bruce, A. J., Ritchie, C. W., Blizard, R., Lai, R. & Raven, P. The incidence of delirium associated with orthopedic surgery: A meta-analytic review. Int. Psychogeriatr. 19, 197–214. https://doi.org/10.1017/S104161020600425X (2007).
4. Agency for Healthcare Research and Quality. HCUPnet. Healthcare Cost and Utilization Project (HCUP). http://hcupnet.ahrq.gov/external (2012).
5. Rizk, P., Morris, W., Oleaje, P. & Huo, M. Review of postoperative delirium in geriatric patients undergoing hip surgery. Geriatr. Orthop. Surg. Rehabil. 7, 100–105. https://doi.org/10.1177/2151458516641162 (2016).
6. Guo, Y. et al. Prevalence and risk factors of postoperative delirium in elderly hip fracture patients. J. Int. Med. Res. 44, 317–327. https://doi.org/10.1177/0300060516624936 (2016).
7. Costa-Martins, I. et al. Post-operative delirium in older hip fracture patients: A new onset or was it already there?. Eur. Geriatr. Med. 12, 777–785. https://doi.org/10.1007/s41999-021-00456-w (2021).
8. Blom, B. L, van Die, H. S., Simon, M. P. & Willems, W. J. The relationship between surgical delay for a hip fracture and the complication risk. Ned. Tijdschr. Geneeskd. 151, 2050–2054 (2007).
9. Freter, S., Dunbar, M., Kolier, K., Macknight, C. & Rockwood, K. Prevalence and characteristics of pre-operative delirium in hip fracture patients. Gerontology 62, 396–400. https://doi.org/10.1159/000442385 (2016).
10. Piolli, G. et al. Surgical delay is a risk factor of delirium in hip fracture patients with mild-moderate cognitive impairment. Aging Clin. Exp. Res. 31, 41–47. https://doi.org/10.1007/s40520-018-0985-y (2019).
11. Agrawal, S., Turk, R., Burton, B. N., Ingrande, J. & Galan, R. A. The association of preoperative delirium with postoperative outcomes following hip surgery in the elderly. J. Clin. Anesth. 60, 28–33. https://doi.org/10.1016/j.jclinane.2019.08.015 (2020).
12. Edlund, A., Lundstrom, M., Brannstrom, B., Bucht, G. & Gustafson, Y. Delirium before and after operation for femoral neck fracture. J. Am. Geriatr. Soc. 49, 1335–1340. https://doi.org/10.1534journals.4.2153-5415.2001.49261.x (2001).
13. Adusumli, A., Levy, R., Heim, M., Mizrahi, E. & Arad, M. The unfavorable nature of preoperative delirium in elderly hip fracture patients. Arch. Gerontol. Geriatr. 36, 67–74. https://doi.org/10.1016/j.dengero.00908-4 (2003).
14. Bellelli, G. et al. Under-detection of delirium and impact of neurocognitive deficits on in-hospital mortality among acute geriatric and medical wards. Eur. J. Intern. Med. 26, 696–704. https://doi.org/10.1016/j.ejim.2015.08.006 (2015).
15. Pilotto, A. et al. A multidimensional approach to frailty in older people. Ageing Res. Rev. 60, 101047. https://doi.org/10.1016/j.arr.2020.101047 (2020).
16. Julebo, V. et al. Risk factors for preoperative and postoperative delirium in elderly patients with hip fracture. J. Am. Geriatr. Soc. 57, 1534–1561. https://doi.org/10.1111/j.1532-5415.2009.02377.x (2009).
17. Vitale, E. et al. Orthopedic multidimensional prognostic index (Ortho-MPI) in the elderly with hip or neck femur fracture: A pilot study. Arch. Gerontol. Geriatr. 58, 101–104. https://doi.org/10.1016/j.jagger.2013.08.006 (2014).
18. von Elm, E. et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. J. Clin. Epidemiol. 61, 344–349. https://doi.org/10.1016/j.jclinepi.2007.11.008 (2008).
19. Katz, S., Downs, T. D., Cash, H. R. & Grotz, R. C. Progress in development of the index of ADL. Gerontologist 10, 20–30. https://doi.org/10.1093/geront/10.1_part_1.20 (1970).
20. Lawton, M. P. & Brody, E. M. Assessment of older people: Self-maintaining and instrumental activities of daily living. Gerontologist 9, 179–186 (1969).
21. Pfeiffer, E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. J. Am. Geriatr. Soc. 23, 433–441. https://doi.org/10.1111/j.1532-5415.1975.tb00927.x (1975).
22. Rubenstein, L. Z., Harker, J. O., Salva, A., Guigoz, Y. & Vellas, B. Screening for undernutrition in geriatric practice: Developing the short-form mini-nutritional assessment (MNA-SF). J. Gerontol. A Biol. Sci. Med. Sci. 56, M366-372. https://doi.org/10.1093/jgerona/56.6.M366 (2001).
23. Bliss, M. R., McLaren, R. & Exton-Smith, A. N. Mattresses for preventing pressure sores in geriatric patients. Mon. Bull. Minist. Health Public Health Lab. Serv. 25, 238–268 (1966).
24. Linn, B. S., Linn, M. W. & Gurel, I. Cumulative illness rating scale. J. Am. Geriatr. Soc. 16, 622–626. https://doi.org/10.1111/j.1532-5415.1968.tb00203.x (1968).
25. Pilotto, A. et al. Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. Rejuvenation Res. 11, 151–161. https://doi.org/10.1089/rej.2007.0569 (2008).
26. Bellelli, G. et al. Validation of the 4AT, a new instrument for rapid delirium screening: A study in 234 hospitalised older people. Age and Ageing 43, 496–502. https://doi.org/10.1093/ageing/aft021 (2014).
27. Panula, J. et al. Mortality and cause of death in hip fracture patients aged 65 or older: A Population-based study. BMC Musculoskelet. Disord. 12, 105. https://doi.org/10.1186/1471-2474-12-105 (2011).
28. Inouye, S. K. Predisposing and precipitating factors for delirium in hospitalized older patients. Dement Geriatr. Cogn. Disord. 10, 393–400. https://doi.org/10.1159/00017177 (1999).
29. Kalsiusvaart, E. J. et al. Risk factors and prediction of postoperative delirium in elderly hip-surgery patients: Implementation and validation of a medical risk factor model. J. Am. Geriatr. Soc. 54, 817–822. https://doi.org/10.1111/j.1532-5415.2006.00704.x (2006).
30. Smith, T. O. et al. Factors predicting incidence of post-operative delirium in older people following hip fracture surgery: A systematic review and meta-analysis. Int. J. Geriatr. Psychiatry 32, 386–396. https://doi.org/10.1002/gps.4655 (2017).
31. van Meenen, L. C., van Meenen, D. M., de Rooy, S. E. & ter Riet, G. Risk prediction models for postoperative delirium: A systematic review and meta-analysis. J. Am. Geriatr. Soc. 62, 2383–2390. https://doi.org/10.1111/jgs.13138 (2014).
32. Chen, X., Lao, Y., Zhang, Y., Qiao, L. & Zhuang, Y. Risk predictive models for delirium in the intensive care unit: A systematic review and meta-analysis. Ann. Palliat. Med. 10, 1467. https://doi.org/10.21037/apm-20-1183 (2021).
33. Moerman, S. et al. Validation of the risk model for delirium in hip fracture patients. Gen. Hosp. Psychiatry 34, 153–159. https://doi.org/10.1016/j.genhosppsych.2011.11.011 (2012).
34. Oberai, T. et al. Development of a postoperative delirium risk scoring tool using data from the Australian and New Zealand Hip Fracture Registry: An analysis of 6672 patients 2017–2018. Arch. Gerontol. Geriatr. 94, 104368. https://doi.org/10.1016/j.archger.2021.104368 (2021).
35. Oosterhoff, J. H. F. et al. Prediction of postoperative delirium in geriatric hip fracture patients: A clinical prediction model using machine learning algorithms. Geriatr. Orthop. Surg. Rehabil. 12, 21514593211062276. https://doi.org/10.1177/2151459321106227 (2021).
36. Freter, S., Dunbar, M., Koller, K., MacKnight, C. & Rockwood, K. Risk of pre-and post-operative delirium and the delirium elderly at risk (DEAR) tool in hip fracture patients. Can. Geriatr. J. 18, 212–216. https://doi.org/10.5770/cgil.18.185 (2015).

Author contributions
A.P. conceived and designed the study; M.P. performed the statistical analysis and takes responsibility of the accuracy of data analysis; C.M. and C.C. interpreted the data and wrote the manuscript; M.R., R.R., A.D., and D.T. contributed in data collection and literature search; M.S. and A.B. assisted in study design and data interpretation; C.S. and A.P. critically revised the final manuscript. All authors approved the final draft submitted. The publication has been approved by all coauthors.

Funding
No funding was received for conducting this study.

Competing interests
The authors declare no competing interests.

Additional information
Correspondence and requests for materials should be addressed to A.P.
