

Comprehensive geriatric care reduces acute perioperative delirium in elderly patients with hip fractures

A meta-analysis

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Abstract

Background: The aim of the current meta-analysis was to assess the treatment effect of comprehensive geriatric care in reducing acute perioperative delirium in older patients with hip fractures, compared with the effect of a routine orthopedic treatment protocol.

Methods: We conducted a search of multiple databases to identify randomized controlled trials (RCTs) and quasi-RCTs comparing comprehensive geriatric care and routine orthopedic treatment regarding the following outcomes: incidence of delirium, assessment of cognitive status, and duration of delirium. Odds ratios (ORs) and mean differences (MDs) were pooled using either a fixed-effects or a random-effects model, depending on the heterogeneity of the trials included in the analysis.

Results: Six RCTs and 1 quasi-RCT provided data from 1840 patients. These data revealed that comprehensive geriatric care may reduce the incidence of perioperative delirium (OR=0.71; 95% confidence interval [CI], 0.57–0.89; $P=.003$) and that it was associated with higher cognitive status during hospitalization or at 1 month postoperatively (MD=1.03; 95% CI, 0.93–1.13; $P\leq .00001$). There was no significant difference in duration of perioperative delirium between the 2 treatment groups (MD=−2.48; 95% CI, −7.36 to 2.40; $P=.32$).

Conclusion: Based on the quality of evidence provided, comprehensive geriatric care may reduce the incidence of perioperative delirium. To obtain evidence regarding the merits of comprehensive geriatric care in reducing severity of delirium and shortening the duration of delirium, there is a need for multicenter RCTs with high methodological quality.

Abbreviations: CAM = Confusion Assessment Method, CI = confidence interval, MD = mean difference, MMSE = Mini Mental State Examination, OBS-Scale = Organic Brain Syndrome Scale, OR = odds ratio, RCT = randomized controlled trial.

Keywords: cognition disorders, comprehensive geriatric care, delirium, geriatric ward, hip fractures, interdisciplinary, multidisciplinary

1. Introduction

Femoral neck fractures and intertrochanteric fractures are frequently sustained by geriatric patients.^[1,2] To reduce compli-

cations, such as decubitus ulcer and hypostatic pneumonia, surgical treatment is mandatory in these fragile patients.^[3–5] With the development of knowledge of biomechanics of osteoporotic proximal femur fractures, expertise of surgical skills, and anesthesia monitoring during surgery, most fragile patients could survive the operation and acquire walking ability.^[6–9] However, quality of life in these patients is deteriorated in comparison with their preinjury level.^[10–13] Acute perioperative delirium, a neuropsychiatric syndrome characterized by disturbance in consciousness, change in cognition, or perceptual disturbance,^[14] is a common complication in geriatric hip-fracture patients;^[14–17] accordingly, patients with delirium require around-the-clock surveillance to prevent accidents. Perioperative delirium is also a predictive risk factor for postoperative mortality, morbidity, poor functional outcomes, and long hospital stay.^[16–19]

Although there has been significant improvement in surgical techniques and skills, perioperative delirium is still high due to orthopedic surgeons' lack of knowledge and experience in managing fragile older patients.^[20] It is presumed that there are several underlying causes that could predispose older patients with hip fractures to perioperative delirium, such as perioperative hypotension, hypoxemia, and anemia.^[21–23] Timely and effective management of these risk factors and geriatric patients' comorbidities may reduce acute perioperative delirium in elderly patients with hip fractures. Comprehensive geriatric care is an established good practice for older trauma patients and incorporates

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multidisciplinary medical specialists.^[24,25] Notwithstanding, several meta-analyses reported contradictory results regarding the treatment effect of comprehensive geriatric care on functional outcomes, length of hospital stay, and mortality rate in older patients with hip fractures.^[20,26–28] However, none of these meta-analyses reported outcomes concerning perioperative delirium. Accordingly, we performed this meta-analysis to compare the treatment effect of comprehensive geriatric care in reducing acute perioperative delirium in older patients with hip fractures with that of routine orthopedic treatment.

2. Materials and methods

2.1. Search strategy

Ethical approval was not necessary for this meta-analysis study. A search of PubMed, Cochrane databases, Database of Promoting Health Effectiveness Review, EPPI-Centre database of health promotion research, Physiotherapy Evidence Database, DissOnline, the European Association for Grey Literature Exploitation, and China National Knowledge Infrastructure was performed from their inception to July 2016, without limitations to the study designs, using the following Medical Subject Heading terms and text words in different combinations (Supplemental file 1, <http://links.lww.com/MD/B766>): geriatrics, geriatric nursing, geriatric psychiatry, health services for the aged, multidisciplinary, comanagement, co-management, interdisciplinary, comprehensive care, geriatr*, geriatr*-orthop*, orthopaedic-geriatr*, ortho*-geriatr*, orthogeriatr*, team approach, protocol driven, integrated care, multi-factorial, hip fracture*, femur* neck fracture*, femoral* neck fracture*, proximal femur* fracture*, proximal femoral* fracture*, intracapsular femur* neck fracture*, intracapsular* femoral* neck fracture*, intracapsular* hip* fracture*, trochant* fracture*, pertrochant* fracture*, intertrochant* fracture*, subtrochant* fracture*, and extracapsular* fracture*. These subject-specific terms were combined with the Cochrane Highly Sensitive Search Strategy, sensitivity- and precision-maximizing version,^[29] to identify randomized controlled trials (RCTs) and quasi-RCTs. The search was supplemented by a manual citation search of the reference lists of relevant studies identified.

2.2. Inclusion criteria/exclusion criteria

Only RCTs and quasi-RCTs were included in our meta-analysis, with nonrandomized trials excluded. All RCTs and quasi-RCTs comparing comprehensive geriatric care to routine orthopedic treatment protocol for hip fracture patients treated in an acute setting were eligible. The patients in the comprehensive geriatric care group needed to be treated by a specialist medical team specializing in geriatric orthopedic patients, with staff providing comprehensive medical assessment, management, and initiation of rehabilitation, and orthopedic surgeons performing the operations. Patients in the routine orthopedic treatment group needed to be cared for by orthopedic surgeons, with geriatric consultation as required. Comprehensive geriatric care treatment needed to be initiated preoperatively or within 24 hours postoperatively.

2.3. Outcomes of interest

The following perioperative outcomes of interest were included in the analysis: incidence of delirium, assessment of cognitive status, and duration of delirium. Delirium was defined as neuropsychiatric

syndrome characterized by disturbance in consciousness (impaired ability to focus, sustain, or shift attention) and change in cognition (memory impairment, disorientation, or language disturbance) or perceptual disturbance (misinterpretations, illusions, or hallucinations); the disturbance needed to occur over a short period and fluctuate during the course of the day.^[16] All outcomes were determined during hospitalization and/or 1 month postoperatively.

2.4. Study selection and data extraction

Two reviewers independently assessed the eligibility of identified trials in an unblinded, standardized manner. Data were collected independently by the 2 reviewers, and disagreements were resolved by discussion with a senior author. The following information was extracted from the included trials: research method; characteristics of trial participants, including age, sex, and fracture type; inclusion and exclusion criteria; intervention characteristics; postoperative outcomes of interest; and risk of bias. When information was missing, we attempted to contact the primary author by email to seek clarification.

2.5. Quality assessment

The risk of bias was evaluated independently by 2 of the review authors using the domain-based evaluation described in the Cochrane Handbook for Systematic Reviews of Interventions.^[30] The following domains were assessed: random sequence generation; allocation concealment; blinding of participants, research personnel, and outcome assessors; incomplete outcome data; and selective outcome reporting. Each of these criteria were assessed as “low risk of bias”, “high risk of bias”, or “unclear risk of bias”, when there was lack of information or uncertainty over the potential for bias. The quality of the evidence was quantified using the Grades of Recommendation, Assessment, Development, and Evaluation approach,^[31] with disagreements between the review authors regarding the risk of bias for the identified domains resolved by consensus.

2.6. Statistical analysis

The meta-analyses were performed using Review Manager software (RevMan Version 5.3; The Nordic Cochrane Center, Copenhagen, Denmark). In addition, tests for funnel plot asymmetry were performed with Stata software (StataSE 12.0; StataCorp LP, College Station, TX). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for dichotomous outcomes. Continuous outcomes were expressed as mean differences (MDs) with corresponding 95% CIs. Heterogeneity across trials was tested by using chi-squared analysis, with the I^2 statistic used to assess the impact of identified heterogeneity on the meta-analysis. Substantial heterogeneity was defined as $I^2 > 50\%$. If substantial heterogeneity between trials included in an analysis was identified, estimates of pooled data were evaluated using a random-effect model; otherwise, a fixed-effect model was chosen. Funnel plot asymmetry was assessed using Begg and Egger tests.

3. Results

3.1. Literature search

The details of our search strategy and exclusion criteria are presented in the flow diagram in Figure 1. A total of 1055 titles and abstracts were preliminarily screened, with 7 trials eventually satisfying our eligibility criteria.^[32–38] We further manually

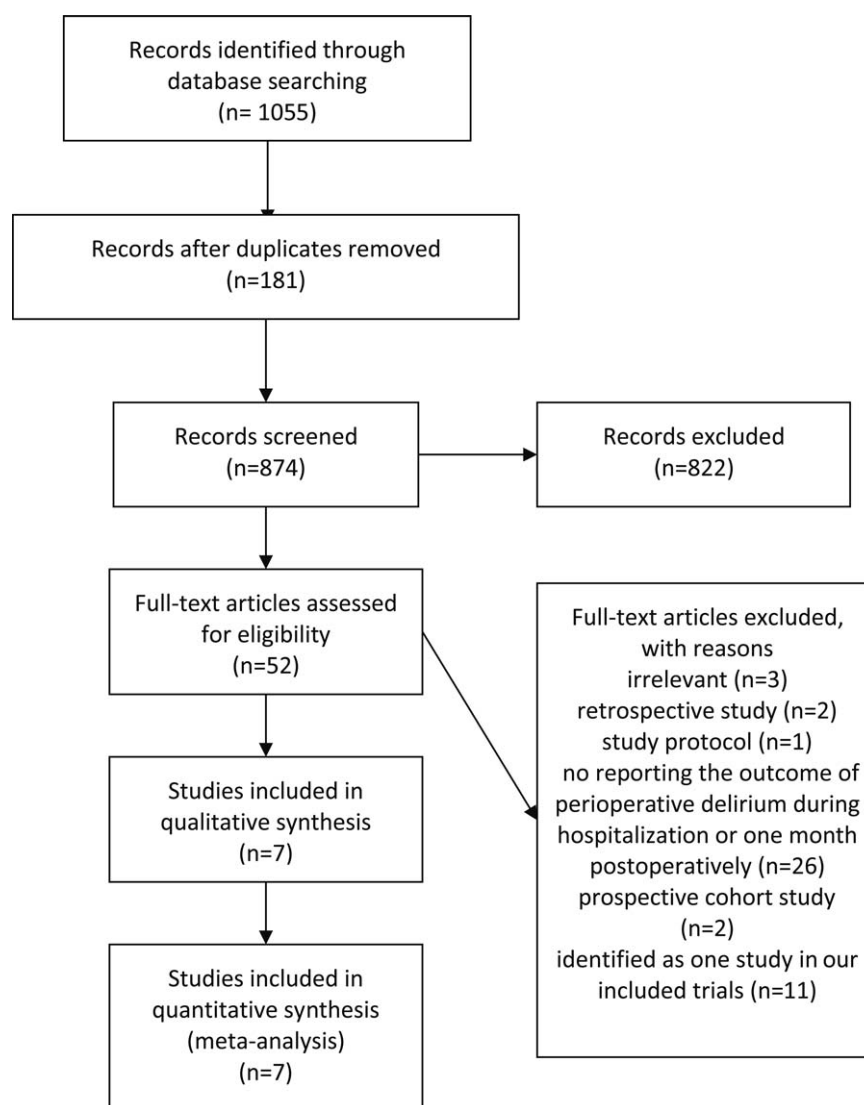


Figure 1. Flow diagram of literature search.

searched the references of the included studies, but identified no more RCTs or quasi-RCTs satisfying our eligibility criteria. We also further investigated the trials not reporting the outcomes of interest; several studies evaluated cognitive status or mental disability using the Mini Mental State Examination (MMSE), Confusion Assessment Method (CAM), Delirium Index, Short Mental Status Questionnaire score, Clinical Dementia Rating Scale, or Red Cross Hospital Scale at the initial admission as participant baseline characteristics.^[25,39–48] Further, we found that 2 studies evaluated general mental health using the Medical Outcomes study 36-item short form Taiwan version shortly after operative treatment of hip fractures, and 1 study evaluated depressive symptoms using the Chinese version of the Geriatric Depression Scale, short form.^[49–51] Nonetheless, none of the aforementioned studies addressed outcomes of acute perioperative delirium during hospitalization or 1 month postoperatively. After thorough discussion with each other and in consultation with a neurology specialist, we decided to exclude these trials to ensure that the definition of acute perioperative delirium strictly adhered to our eligibility criteria and consistent

throughout our included trials. Six of the included trials were RCTs,^[32–37] and 1 was a quasi-RCT.^[38] Each study reported the outcome of treatment effect of comprehensive geriatric care in reducing acute perioperative delirium in older patients with hip fractures, compared with that of routine orthopedic treatment.

3.2. Quality assessment

Six included studies had methodological flaws that put them at either unclear or high risk of bias for at least 1 domain,^[32–35,37,38] with 1 trial of high methodological quality^[36] (Figs. 2 and 3). Adequate randomization was reported in 4 RCTs; these RCTs used a random number table,^[36] computer-generated number,^[32,35] or throw of dice^[34] as randomization methods. The method of randomization was not reported in the other 2 RCTs^[33,37]. The quasi-RCT reported that group assignment was based on bed availability.^[38]

Three trials described the method of allocation concealment.^[32,36,37] Two studies used blinding of participants,

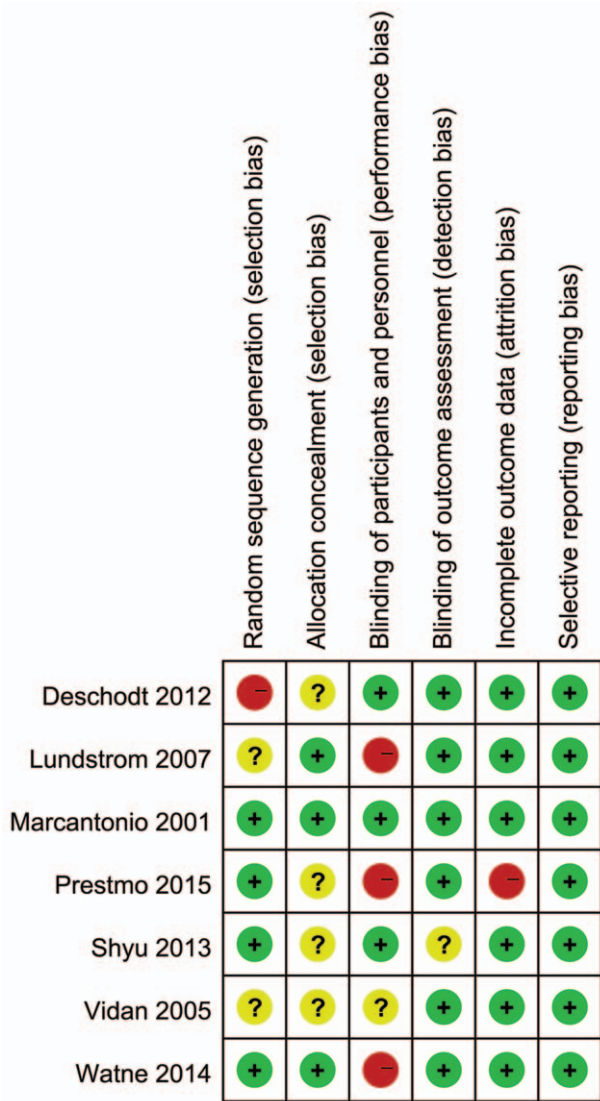


Figure 2. Summary of risk bias assessment. *Note:* Reviewers' assessment of each risk of bias item; "+", low risk of bias; "?", unclear risk of bias; and "-", high risk of bias.

personnel and outcome assessment,^[36,38] 1 trial used blinding of participants and personnel,^[34] and 4 trials used blinding of outcome assessment.^[32,33,35,37] One study was at high risk of bias from incomplete outcome data, this was due to a high attrition

rate (19.40%); furthermore, the authors did not report the derivation of missing data, nor did they describe the distribution of patients lost to follow-up between the 2 treatment groups. Moreover, that particular study reported the cognitive status evaluated by MMSE, without the outcomes of incidence of delirium or duration of delirium.^[35]

3.3. Descriptive characteristics

The descriptive characteristics of the included studies are listed in Table 1, with relevant characteristics summarized here. All the included trials were reported in English and were single-center trials; 5 trials were conducted in Europe,^[32,33,35,37,38] 1 in North America,^[36] and 1 in China.^[34] Six studies were parallel RCTs^[32-37] and 1 was a quasi-RCT.^[38] In 4 of the included studies, the patients in the comprehensive geriatric care group were actively cared for by a geriatric team daily^[33,34,36,38]; in the other 3 trials, the patients in the comprehensive geriatric care group were cared for in the geriatric ward.^[32,35,37] Five studies initiated the comprehensive geriatric care treatment preoperatively,^[32-35,38] 1 study initiated the treatment within 24 hours postoperatively,^[37] and 1 study initiated the treatment either preoperatively or within 24 hours postoperatively.^[36] Six studies reported no significant difference in preoperative cognitive status between treatment groups,^[32,33,35-38] with 1 study excluding cognitively impaired participants.^[34]

Together, the included trials enrolled a total of 1840 patients; after accounting for participants lost to follow-up, data from 1763 participants were entered in our meta-analysis. Six trials included hip fractures (extra- and intracapsular),^[32-36,38] and 1 trial included only femoral neck fractures.^[37]

3.4. Effects of interventions

Four trials coincidentally and strictly followed the CAM criteria to diagnose perioperative delirium.^[32,33,36,38] One trial used the Organic Brain Syndrome Scale (OBS-Scale) to screen the patients for perioperative deliriums; the authors stated that the OBS-Scale showed 100% agreement regarding the diagnosis of delirium when compared with the CAM.^[37] One trial did not directly screen the participants for delirium, but detected perioperative delirium using the MMSE.^[34] Six trials reported the incidence of perioperative delirium during hospitalization or at 1 month postoperatively,^[32-34,36-38] with a calculated OR of 0.71 (95% CI, 0.57-0.89; $P = .003$; Fig. 4). Four trials reported the number of days of perioperative delirium,^[32,36-38] but we were only able to extract data from 2 trials,^[36,37] with a calculated MD of -2.48 (95% CI, -7.36 to 2.40; $P = .32$; Fig. 5). The other 2 trials

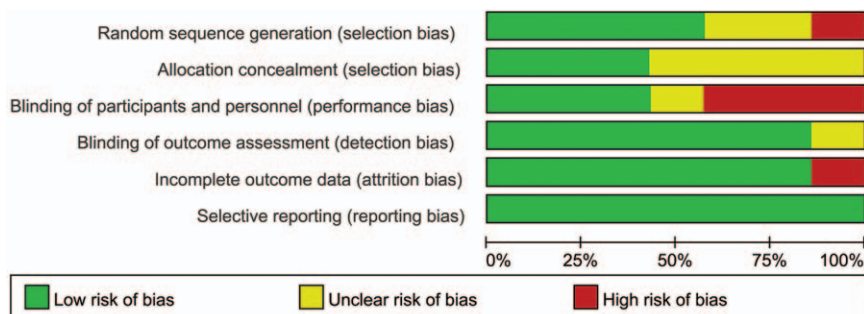


Figure 3. Risk of bias graph. *Note:* Reviewers' assessment of each risk bias item, presented as a percent across all included randomized controlled trials.

Table 1
Descriptive characteristics of included trials.

| Study ID | Country | Sample size (intervention) | Sample size (control) | Age (intervention) | Age (control) | Sex (M/F) (intervention) | Sex (M/F) (control) | Lost to follow-up | Funding | Trial registration |
|------------------|---------|----------------------------|-----------------------|--------------------|---------------|--------------------------|---------------------|-------------------|---------|--------------------|
| Watne 2014 | Norway | 163 | 166 | 84 (55–99)* | 85 (46–101) | 42/121 | 38/128 | 0 | Yes | Yes |
| Vidan 2005 | Spain | 155 | 164 | 81.0 ± 7.8† | 82.6 ± 7.4 | 24/131 | 35/129 | 0 | Yes | No |
| Shyu 2013 | China | 200 | 99 | 73.3 ± 6.9 | 76.9 ± 8.2 | 73/127 | 35/64 | 0 | Yes | No |
| Prestmo 2015 | Norway | 198 | 199 | 83.4 ± 5.4 | 83.2 ± 6.4 | 53/145 | 51/148 | 77 | Yes | Yes |
| Marcantonio 2001 | USA | 62 | 64 | 78.0 ± 8.0 | 80.0 ± 8.0 | 13/49 | 14/50 | 0 | Yes | No |
| Lundstrom 2007 | Sweden | 102 | 97 | 82.3 ± 6.6 | 82.0 ± 5.6 | 28/74 | 23/74 | 0 | Yes | No |
| Deschodt 2012 | Belgium | 94 | 77 | 80.4 ± 7.0 | 81.1 ± 7.2 | 25/69 | 20/57 | 0 | No | No |

* Median (range).
† Mean ± SD (standard deviation).

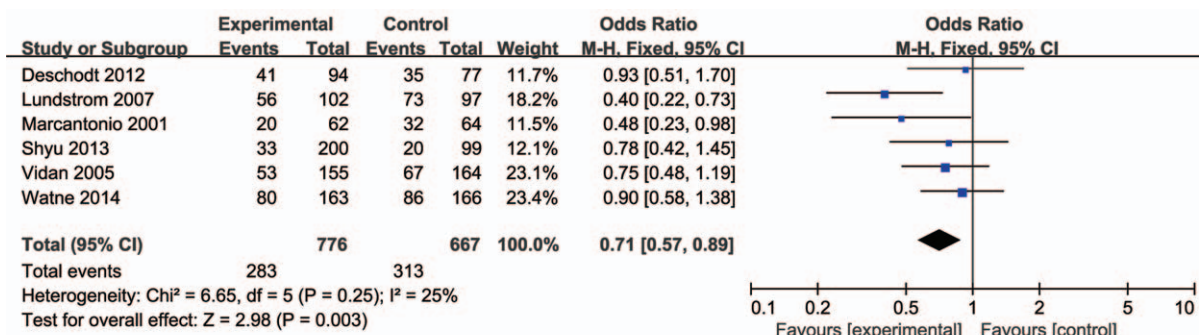


Figure 4. Forest plot of odds ratios and associated confidence intervals for the incidence of perioperative delirium during hospitalization or 1 month postoperatively.

reported the median duration of delirium,^[32,38] with no significant differences between groups.

Three trials assessed cognitive status during hospitalization or at 1 month postoperatively using the MMSE^[35,37,38]; we were only able to extract data from 2 trials,^[35,37] with a calculated MD of 1.03 (95% CI, 0.93–1.13; $P < .00001$; Fig. 6). The remaining trial^[38] reported that control participants

had lower MMSE scores than those in intervention participants.

3.5. Sensitivity analysis

As 1 study used the MMSE to diagnose delirium indirectly^[34] and 5 trials used a more sophisticated screening method,^[32,33,36–38] we

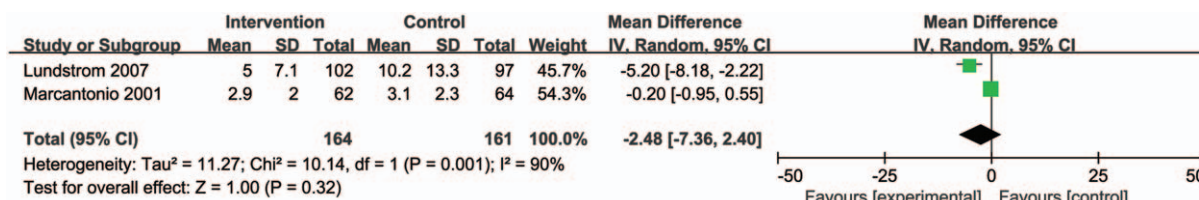


Figure 5. Forest plot of mean differences and associated confidence intervals for number of days of perioperative delirium during hospitalization or 1 month postoperatively.

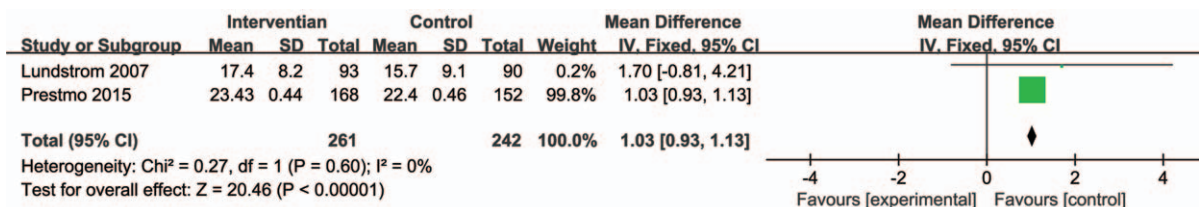


Figure 6. Forest plot of mean differences and associated confidence intervals for cognitive status based on Mini-Mental State Examination Scores during hospitalization or 1 month postoperatively.

performed the sensitivity analysis by excluding the study using the MMSE. The result was in accordance with general pooled data, with a calculated OR of 0.71 (95% CI, 0.56–0.89; $P = .004$).

3.6. Publication bias

An assessment of publication bias was conducted for incidence of perioperative delirium; the funnel plot is presented as Supplemental file 2, <http://links.lww.com/MD/B766>. The analysis did not identify any potential publication bias (Egger test, $P = .250$; Begg test, $P = .260$).

4. Discussion

The current meta-analysis indicated that being in the comprehensive geriatric care group was associated with a lower incidence of perioperative delirium and higher cognitive status during hospitalization or at 1 month postoperatively. There was no significant difference in duration of perioperative delirium between the 2 groups. Although we could not extract outcome data from 3 trials which reported cognitive status and duration of perioperative delirium, the results of these 3 trials were in accordance with our pooled results.

Delirium is the frequently encountered complication in elderly hip fracture patients by orthopedic surgeons, but it received much less attention compared with other complications, such as deep vein thrombosis, pulmonary embolism, and infections. The pathogenesis of delirium has not been thoroughly studied and fully understood. It has been reported that there are several underlying causes which predisposing geriatric hip fracture patients to perioperative delirium. Timely and corrective management of these underlying causes and patient comorbidities may reduce perioperative delirium in elderly hip fracture patients. Although multiple meta-analyses reported the treatment effect of comprehensive geriatric care compared with routine orthopedic treatment, the result of perioperative delirium has not been reported yet. Our meta-analysis exclusively focuses on the treatment effect of comprehensive geriatric care on perioperative delirium to complement existing meta-analyses.

Our meta-analysis included 7 studies which reported outcomes of interest concerning perioperative delirium. Because the outcome of interest was delirium during hospitalization or at 1 month postoperatively, attrition bias was low in 6 included studies due to the short-term follow-up period, with only 1 trial high attrition bias. Due to lack of allocation concealment and blinding of participants and personnel, we concluded the quality of evidence for incidence of perioperative delirium to be moderate. With regard to cognitive status, owing to the lack of blinding of participants and personnel in combination with the low sample size and high attrition bias, we concluded the quality of evidence for perioperative cognitive status was very low. Due to high heterogeneity and low sample size, we concluded the quality of data regarding duration of delirium to be low.

The current meta-analysis firmly followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for systematic reviews and meta-analyses (Supplemental file 3, <http://links.lww.com/MD/B766>). However, there are several limitations, so the outcomes should be interpreted with caution. First, all the included studies were small, single-center trials. Second, the included studies used 3 diagnosis and assessment criteria to screen participants for acute perioperative delirium; of these, the CAM and OBS-Scale are validated in the literature in assessing and diagnosing delirium with high sensitivity and

specificity,^[52,53] whereas MMSE has been used but is not frequently used in diagnosing delirium.^[54] Accordingly, we performed the sensitivity analysis by excluding the study of Shyu et al,^[34] in which delirium was diagnosed using MMSE and in which the incidence of acute of perioperative delirium was much lower than other included studies. The result was in accordance with general pooled data. Third, although comprehensive geriatric care in our identified trials coincidentally included treatment provided by a specialist medical team specializing in geriatric orthopedic patients, the specific intervention, surgical technique, staff member experience, and anesthetic method would differ between studies. Fourth, the inclusion and exclusion criteria were different across included trials, and the differences in included/excluded comorbidities may affect our outcome of interest. Fifth, because of a language barrier, we excluded studies written in languages other than English and Chinese. We acknowledge that failure to include studies in other languages resulted in missing data.

5. Conclusion

The present meta-analysis is the first to assess the treatment effect of comprehensive geriatric care in reducing perioperative delirium in older patients with hip fractures compared with the effect of a routine orthopedic treatment protocol. Based on the quality of evidence provided, comprehensive geriatric care can reduce the incidence of perioperative delirium during hospitalization or at 1 month postoperatively. To obtain evidence regarding the merits of comprehensive geriatric care in reducing severity of delirium and shortening the duration of delirium, there is a need for multicenter RCTs with high methodological quality.

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