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REVIEW

The role of perioperative oral nutritional supplementation in elderly patients after hip surgery

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Background: The effect of perioperative oral nutritional supplementation (ONS) on elderly patients after hip surgery remains controversial. This study intended to ascertain whether perioperative ONS is beneficial for the rehabilitation of elderly patients after hip surgery.

Materials and methods: We searched databases including PubMed, Embase, and the Cochrane Central Register of Controlled Trials for articles published up to May 2014. Randomized controlled trials of ONS for elderly patients after hip surgery were included.

Results: The combined trials showed that ONS had a positive effect on the serum total protein ($P<0.00001$) and led to a significantly decreased number of complications ($P=0.0005$). Furthermore, data from the infection subgroups showed significant decreases in wound infection ($P=0.02$), respiratory infection ($P=0.04$), and urinary tract infection ($P=0.03$). Clinical observation suggests that the intervention may improve the level of serum albumin, although the data did not reach statistical significance ($P=0.48$). Regarding mortality, there was no significant statistical difference between the intervention group and the control ($P=0.93$).

Conclusion: Based on the evidence available, this meta-analysis is consistent with the hypothesis that perioperative ONS can help elderly patients recover after hip surgery and reduce complications.

Keywords: oral nutrition, elderly patient, hip surgery, meta-analysis

Introduction

The incidence of hip fracture in elderly people will reach 11.9% by the end of 2030 with life extension and increasing social activities such as travelling, riding (bicycle and motorcycle), dancing, and so on.[1–5] Nutritional status is an important influencing factor for early postoperative rehabilitation. However, a variety of factors, such as pre-fracture nutritional status, underlying diseases, and wound stress induce a high incidence of postoperative complications and mortality.[6–8] Moreover, blood loss, postoperative poor appetite, and poor food intake occur regularly among elderly patients in hospital.[9–11] Therefore, clinicians are seeking effective measures which can improve the perioperative nutritional status of elderly patients after hip surgery.[12–14]

Among various nutritional supplement interventions, many studies have proposed that oral nutritional supplementation (ONS) might be a convenient method to enhance energy and protein intake and be beneficial for elderly patients who are undergoing trauma stress reaction from hip fractures or surgeries to improve bowel health and nutrient intake. Furthermore, ONS is more economical and practical than parenteral nutritional supplementation.[15,16] One multicenter, randomized controlled trial (RCT),

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which mainly investigated the cost-effectiveness of intensive nutritional supplementation, found that the cost of oral nutritional intervention is lower than that of other types of nutritional intervention. Meanwhile, cost-effectiveness evaluation showed that the ONS intervention route is more likely to be cost-effective.[16]

While ONS has been increasingly attracting the attention of clinicians, more and more RCTs have been conducted to evaluate the effectiveness of ONS for elderly patients after hip surgery and suggest that ONS is a beneficial intervention for elderly patients after hip surgery to improve the nutritional status.[9,12,13,17,18] However, there remain opposing opinions about the efficiency of ONS. Some researchers have shown that functional recovery and mortality were not statistically improved after ONS intervention in elderly patients after hip surgery,[19–21] while a relevant review mentioned that a definite conclusion about ONS for elderly patients with hip fracture, whether surgery was performed or not, could not be drawn because of weak evidence.[20]

As orthopedic doctors, we are concerned about the management of nutritional status of elderly patients during the perioperative period. Obviously, we wish to have better knowledge about appropriate interventions to reduce complications, shorten the time of hospitalization, and improve the patients' health. Therefore, the aim of this meta-analysis was to determine whether ONS can be recommended as a routine nutritional intervention for elderly patients after hip surgery.

Clinical relevance

It is very important to return the nutritional status back to normal levels in elderly patients aged over 65 years during the perioperative period. Meanwhile, strategy selection should be evidence based. The findings of this meta-analysis on whether perioperative ONS can reduce complications are clinically relevant for clinicians, including emergency physicians, orthopedic surgeons, nursing staff, geriatricians, and rehabilitation physicians, and can help them properly treat elderly patients and effectually improve clinical outcomes.

Materials and methods

Data sources and searches

We searched for relevant articles published up to May 2014 in databases including PubMed, Embase, and the Cochrane Central Register of Controlled Trials. The terms "oral nutrition" or "oral supplement", "hip surgery" or "hip fracture" or "femoral neck fracture" or "intertrochanteric fracture" or "subtrochanteric fracture", and "old" or "elderly" or "aged" were used to search titles, abstracts, and medical subject headings. We also browsed the reference lists and consulted experts to search for potentially eligible studies.

Study identification

The inclusion criteria used in the selection were as follows: 1) target population: patients aged over 65 years who had had hip fractures (femoral neck, intertrochanteric or subtrochanteric, acetabulum fractures) and undergone surgery (open reduction and internal fixation or arthroplasty); 2) intervention measure: perioperative ONS (orally taking high-calorie or high-protein diets); and 3) design type: RCT. The exclusion criteria used in the selection were: 1) patients with multiple systemic fractures or pathologic fractures; 2) data without standard deviations; 3) participants with hip fractures who had undergone nonsurgical treatment.

Quality assessment

We assessed the quality of individual studies by using the validated Oxford Scale and obtaining Jadad scores,[22] which ranged from 1–5 points. Scores of 1–2 were considered as low quality, while scores of 3–5 were considered as high quality. Two independent reviewers performed the initial screening and extraction procedures. Then, another two investigators independently assessed all articles which met the inclusion criteria. Whenever there was a disagreement, it was solved by collective discussion among the investigators.[23]

Main outcomes

We extracted information about the characteristics of the included studies, such as the research design, population of participants, age of participants, fracture classification, follow-up periods, intervention measurements, control measurements, and the assessment criteria. Then, we analyzed each study for its Jadad score.

Data were collected from the included studies, including data for: 1) total protein; 2) complications (including all infections, bed sores, cardiac disease, cognitive impairment, prolonged immobilization, thrombophlebitis, deep vein thrombosis, vomiting, diarrhea, pressure ulcers, dysphasia, severe hyponatremia, anaphylaxis, pneumonedema, pulmonary embolism, and myocardial infarction); 3) change in serum albumin levels (the difference in serum albumin levels before and after intervention [g/L]); and 4) mortality.

Data synthesis

Perioperative data regarding the patients, interventions, and outcomes mentioned above were extracted from the

included studies. We used Review Manager 5.1 software to analyze the data and adopted a 95% confidence interval (CI). Two reviewers monitored the data inputting to ensure accuracy. For the measurement outcomes, the mean standard deviation, and n were recorded, and the standard mean difference (SMD) was calculated. For the enumeration outcomes, the scale and the numbers were recorded, then the odds ratio (OR) was calculated.[24,25]

Heterogeneity, sensitivity, and risk of bias

We used I^2 to test heterogeneity and estimate total variation across studies. For I^2, values between 25% and 50% were considered as low heterogeneity; those between 50% and 75% were considered as medium heterogeneity; and those over 75% were considered as high heterogeneity.[23,24,26] We qualitatively assessed each included study for allocation, attrition, and reporting bias, using Stata 11 software to perform the Begg's test.[23,27–29]

Results

Characteristics of included studies

As shown in Figure 1, 57 articles published from 1966 to May 2014 were retrieved. Following the inclusion and exclusion criteria, we eliminated the retrospective studies with historical control, the studies lacking original data or standard deviation analysis, and the research with different evaluation indicators. After reading the full texts, we eliminated the studies that were not RCTs, not full text or relevant to ONS or standard deviation. Finally, ten RCTs[13,14,19,21,30–35] were included; the characteristics of these studies are presented in Table 1. A total of 986 elderly patients who had undergone hip surgery and were aged over 65 years were included. Each of the ten studies was an RCT, and two of them were double blind.[19,33] Further, they all used standard deviation to analyze results.[23] The study quality varied across these trials: six of the ten included studies had Jadad scores of 3–5, while the other four studies scored 1–2.

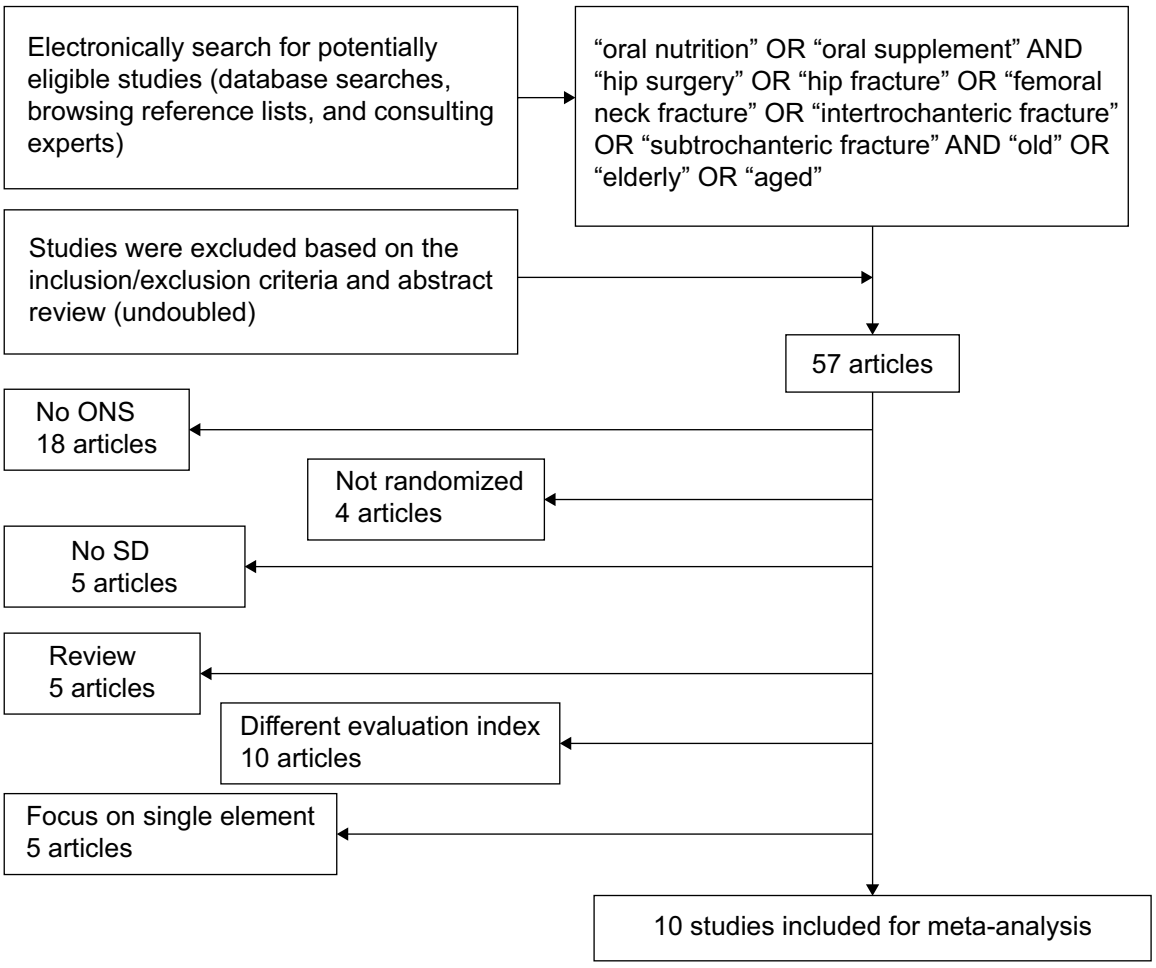

Figure 1 Flow diagram of the selection of studies.
Notes: The flow diagram expounds the studies identified, included, and excluded, as well as the reasons for exclusion. Ten studies were included.
Abbreviations: ONS, oral nutritional supplementation; SD, standard deviation.

Table 1 Characteristics of included trials

Trial, year	Number of participants	Fracture type	Description	Participant age (years)[a]	Follow-up time	Intervention	Control	Evaluation indexes extracted	Methodological rating for concealment of randomization
Stableforth, 1986[41]	61	Femoral neck fracture	Randomized controlled trial	81 (65–96)	1 week	ONS	Normal ward meal	Proteins intake	2
Delmi et al 1990[31]	59	Femoral neck fracture	Randomized controlled trial	82 (61–96)	3 weeks	ONS	Standard hospital diet	Admission serum albumin level,[b] complications, mortality	2
Espaulella et al 2000[33]	171	Hip fracture	Double-blind, randomized, placebo-controlled clinical trial	ONS: 82.4±6.6 (70–101); control: 82.7±6.6 (70–96)	6 months	Oral protein and antioxidants supplement	Placebo	Admission serum albumin and BMI, postoperative Barthel Index, days in hospital, complications, mortality	5
Bruce et al 2003[21]	109	Hip fracture	Randomized controlled trial	ONS: 84.7±7.3; control: 83.3±8.0	1 week	Liquid ONS	No supplement	Admission serum albumin and BMI, postoperative serum albumin and change in serum albumin, change in weight, days in hospital, handgrip strength, mortality	2
Tidermark et al 2004[19]	60	Femoral neck fracture	Randomized controlled trial	83±5	6 and 12 months	Oral protein-rich formula	Standard treatment	Admission serum albumin and BMI, postoperative serum albumin, change in serum albumin, serum CRP, BMI, weight, handgrip strength, complications	5
Neumann et al 2004[35]	46	Hip fracture	Randomized, double-blind, parallel-group study	ONS: 82.7±1.6; control: 83.7±1.5	1 month	Standard diet with high-protein liquid nutritional supplement	Standard diet with regular liquid nutritional supplement	Admission serum albumin and BMI, postoperative change in serum albumin, serum CRP, BMI, weight, protein intake, handgrip strength, complications	2
Miller et al 2006[42]	100	Hip fracture	Randomized controlled trial	≥70	3 months	Oral protein and antioxidants	Usual clinical care	Admission BMI and Barthel Index, postoperative change in weight, gait speed	1
Bottella-Carretero et al 2008[30]	60	Hip fracture	Randomized controlled, open, parallel-group, three-arm clinical trial	83.8±6.6	Hospital discharge	Commercial enteral nutritional supplement for oral intake	No ONS; standard or texture-adapted diet	Admission serum albumin and BMI, complications, days in hospital	5
Bottella-Carretero et al 2010[13]	60	Hip fracture	Randomized controlled, open, parallel-group, two-arm design	ONS: 82.1±7.3; control: 85.1±7.4	Hospital discharge	Energy and protein supplements	Standard or texture-adapted diet	Admission BMI, postoperative complications, days in hospital	3
Cameron et al 2011[17]	44	Hip fracture (65%) or other fractures	Randomized controlled trial	85.3±6.1	5 weeks and 4 months	Additional high-calorie and high-protein supplementation to usual diet	Standard treatment	Admission serum albumin, BMI, and Barthel Index; postoperative serum albumin, BMI, weight, gait velocity, and grip strength	3
Fabian et al 2011[14]	23	Hip fracture	Prospective randomized, placebo-controlled clinical trial	ONS: 85±7; control: 82±8	Hospital discharge and 3 weeks after discharge	Oral protein and antioxidants	Standard medical treatment	Admission serum albumin and BMI, postoperative serum albumin, CRP	2

Notes: [a]Values are mean ± SD or mean (range). [b]As the postoperative serum albumin was not recorded, the admission serum albumin data were excluded. The methodological rating for concealment of randomization scores were assessed using the validated Oxford Scale and obtaining Jadad scores,[22] which ranged from 1–5 points. Scores of 1–2 were considered as low quality, while scores of 3–5 were considered as high quality.

Abbreviations: BMI, body mass index; CRP, C-reactive protein; ONS, oral nutritional supplementation; SD, standard deviation.

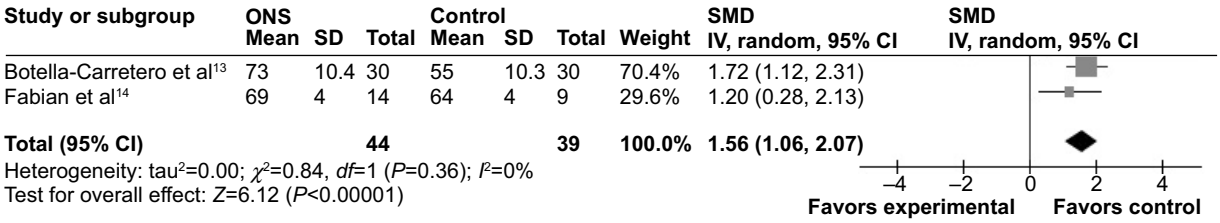

Figure 2 Forest plot for total proteins.
Notes: A random effects analysis model was adopted. The forest plot indicates that there was a significant increase in total protein levels at discharge for the ONS group compared to the control (SMD: 1.56 [95% CI: 1.06, 2.07]; $P<0.00001$). Heterogeneity: $I^2=0\%$; $P=0.36$.
Abbreviations: CI, confidence interval; *df*, degrees of freedom; IV, intravenous; ONS, oral nutritional supplementation; SD, standard deviation; SMD, standard mean difference.

As shown in Table 1, we extracted information about the research design characteristics of the included studies, including the population of participants, age of participants, fracture classification, follow-up period, intervention measurements, control measurements, the comparison of assessment criteria between control group and intervention group, and the Jadad score of each study. Not all evaluation indicators of the included studies were the same, so we merged the data of those studies with the same evaluation indicator to analyze the results.

Total protein

Following the inclusion and exclusion criteria, two studies (Bottella-Carretero et al[13] and Fabian et al[14]) were included. The two studies had a total of 83 patients in the meta-analysis, consisting of 44 patients in the ONS group and 39 in the control group. There was a statistically significant increase of the total protein levels in ONS group before patients were discharged (SMD =1.56 [95% CI: 1.06, 2.07]; $P<0.00001$) (Figure 2). There was no evidence of heterogeneity between the studies ($I^2=0\%$; $P=0.36$).

Complications

Following the inclusion and exclusion criteria, six studies (Tidermark et al,[19] Neumann et al,[35] Espaulella et al,[33] Delmi et al[31] and Bottella-Carretero et al[13,30]) were included in the complications meta-analysis. A total of 463 patients from the six studies were included in the meta-analysis, consisting of 220 patients in the ONS group and 243 in the control group. Figure 3 shows that the ONS had a measurable effect on reducing complications after hip surgery in elderly patients (OR =0.49 [95% CI: 0.32, 0.73]; $P=0.0005$). No evidence of statistical significance for heterogeneity was found among the studies ($I^2=27\%$; $P=0.24$).

Wound infection

Following the inclusion and exclusion criteria, three studies (Bottella-Carretero et al,[13] Delmi et al[31] and Neumann et al[35]) were included in the wound infection meta-analysis. A total of 199 patients from the three studies were included in the meta-analysis, consisting of 97 patients in the ONS group and 102 in the control group. Pooled results indicate that the ONS group had a lower rate of wound infection than

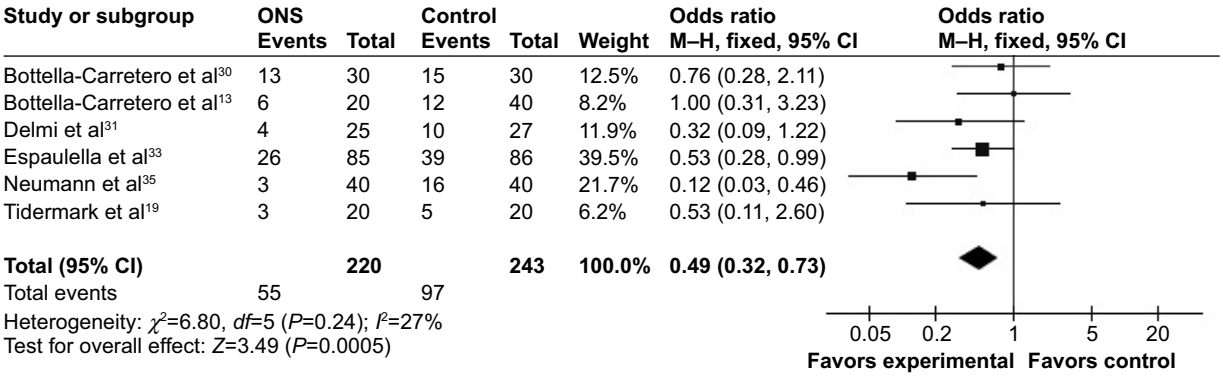

Figure 3 Forest plot for complications.
Notes: This forest plot displays the odds ratios of complications estimated from six cohort studies. The combined data indicate that there were fewer complications in the intervention group compared to the control (OR =0.49 [95% CI: 0.32, 0.73]; $P=0.0005$). Heterogeneity: $I^2=27\%$; $P=0.24$.
Abbreviations: CI, confidence interval; *df*, degrees of freedom; ONS, oral nutritional supplementation; OR, odds ratio; M–H, Mantel–Haenszel.

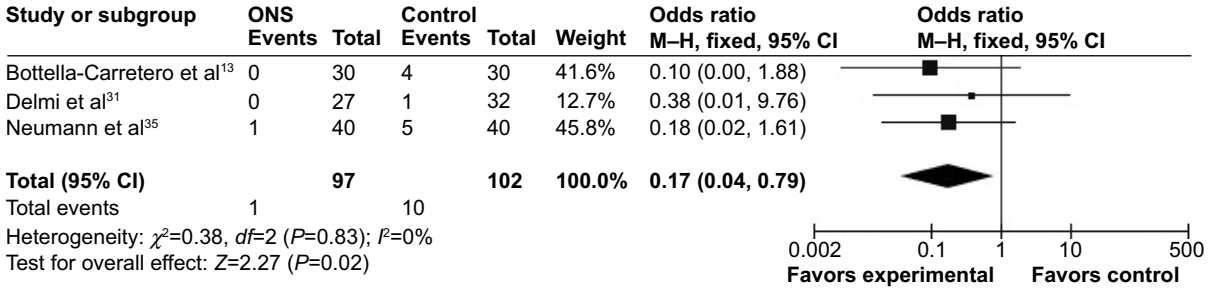

Figure 4 Forest plot for wound infections.
Notes: The forest plot shows the odds ratios of wound infections estimated from three studies. The combined data indicate that there were fewer wound infections in the ONS group compared to the control (OR =0.17 [95% CI: 0.04, 0.79]; *P*=0.02). Heterogeneity: I^2=0%; *P*=0.83.
Abbreviations: CI, confidence interval; *df*, degrees of freedom; ONS, oral nutritional supplementation; M–H, Mantel–Haenszel.

the control group (OR =0.17 [95% CI: 0.04, 0.79]; *P*=0.02). There was no evidence of heterogeneity among the studies (I^2=0%, *P*=0.83) (Figure 4).

Respiratory infection

Following the inclusion and exclusion criteria, three studies (Bottella-Carretero et al,[30] Delmi et al[31] and Neumann et al[35]) were included in the respiratory infection meta-analysis. A total of 200 patients from the three studies were included in the meta-analysis, consisting of 100 patients in the ONS group and 100 in the control group. Figure 5 shows the respiratory infection rates between ONS patients and the control group. According to the three trials included, there were significant statistical difference in the baseline and the length of hospitalization between two groups (OR =0.26 [95% CI: 0.07, 0.94]; *P*=0.04). No statistical significance of heterogeneity was found among the included studies (I^2=21%; *P*=0.28).

Urinary tract infection

Following the inclusion and exclusion criteria, three studies (Bottella-Carretero et al,[30] Delmi et al[31] and Neumann et al[35]) were included in the urinary tract infection meta-analysis. A total of 200 patients from the three studies were included in the meta-analysis. Figure 6 shows the urinary tract infection rates between ONS patients and the control group. Based on the three trials, there were significant differences between the two groups both on baseline and hospitalization time (OR =0.22 [95% CI: 0.05, 0.90]; *P*=0.03). There was no evidence for heterogeneity among the studies (I^2=0%; *P*=0.90).

Change in serum albumin

Following the inclusion and exclusion criteria, data for the change in serum albumin levels from three studies (Bruce et al,[21] Neumann et al[35] and Tidermark et al[19]) were included. These three studies had a total of 172 patients, consisting of 82 patients in the ONS group and 90 in the control group in the meta-analysis. As shown in Figure 7, the change in serum albumin did not have any statistically significant difference between ONS patients and control group (SMD =0.82 [95% CI: −1.47, 3.10]; *P*=0.48). Heterogeneity was found to be large and statistically significant for the change in serum albumin in this analysis (I^2=97%, $P<0.00001$).

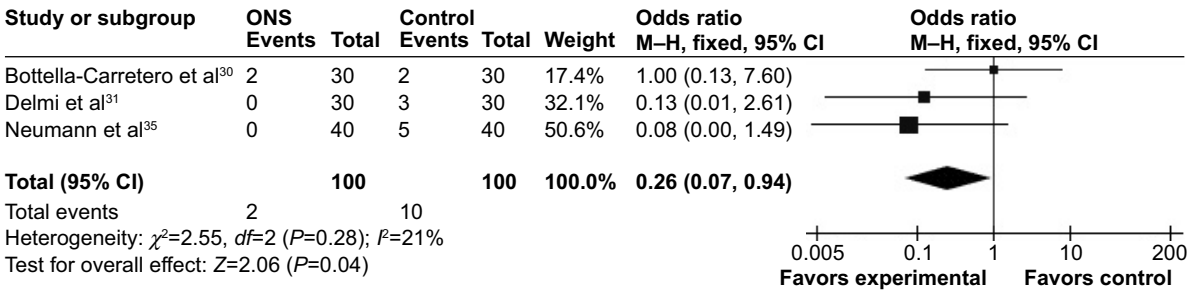

Figure 5 Forest plot for respiratory infections.
Notes: The forest plot shows the odds ratios of respiratory infections estimated from three studies. The combined data indicate that there were fewer respiratory infections in the ONS group compared to the control (OR =0.26 [95% CI: 0.07, 0.94]; *P*=0.04). Heterogeneity: I^2=21%; *P*=0.28.
Abbreviations: CI, confidence interval; *df*, degrees of freedom; ONS, oral nutritional supplementation; M–H, Mantel–Haenszel.

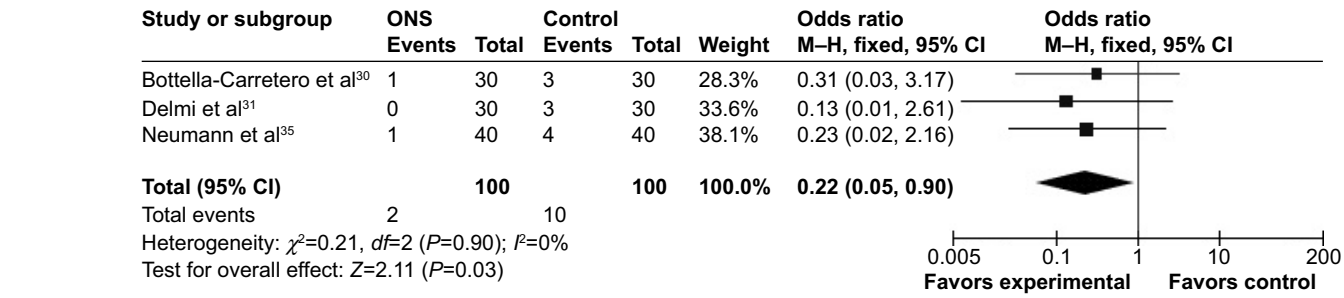

Figure 6 Forest plot for urinary tract infections.
Notes: The forest plot shows the odds ratios of urinary tract infections estimated from three studies. The combined data indicate that there were fewer urinary tract infections in the ONS group compared to the control (OR =0.22 [95% CI: 0.05, 0.90]; *P*=0.03). Heterogeneity: I^2=0%; *P*=0.90.
Abbreviations: CI, confidence interval; *df*, degrees of freedom; ONS, oral nutritional supplementation; M–H, Mantel–Haenszel.

Mortality

Following the inclusion and exclusion criteria, five studies (Bruce et al,[21] Delmi et al,[31] Espaulella et al,[33] Neumann et al[35] and Tidermark et al[19]) were included. The five studies had a total of 416 patients, consisting of 198 patients in the ONS group and 218 in the control group in the meta-analysis. The analysis of mortality indicated that ONS had no statistically significant effect on mortality (ONS group 35/198 versus control group 39/218; OR =1.02 [95% CI: 0.62, 1.70]; *P*=0.93). Large and statistically significant heterogeneity was found in this meta-analysis (I^2=34%; *P*=0.19) (Figure 8).

Assessment of publication bias

As shown in Figure 9, the Begg's funnel plot shows no significant Begg's test for publication bias (*P*>0.05), indicating no evidence of publication bias among the studies.

Discussion

To our knowledge, this is the first meta-analysis assessing studies about elderly patients receiving ONS after hip surgery. The overall results of the current investigation suggest that ONS improves early recovery by increasing the total protein level and reducing complications in elderly patients after hip surgery.

As shown in our meta-analysis, there was a statistically significant improvement in the serum total protein level in the ONS group compared with that in the control group. As a nutritional marker, serum total protein, along with nutrition-rich supplements, helps patients to recover more quickly. Moreover, protein-rich supplementation might further lower blood pressure, improve lipid levels, and reduce estimated cardiovascular risks.[36]

Complications are always directly related to the quality of the patient's lifestyle and the quality of medical services. The incidence of complications (eg, pressure sores, infections, deep venous thromboses, cardiovascular events) in elderly patients after hip surgery is high and deserves more attention. Our study showed the complications rate was lower in elderly patients receiving ONS than in the control group. Similar results were found in previous studies of nasogastric feeding and parenteral nutrition.[13,19,30,31,33,37] Further, we carried out a subgroup analysis on infections (including wound infection, respiratory tract infection, and urinary tract infection), the results of which showed a consistent reduction in each infection rate in the ONS group. The wound infection rate

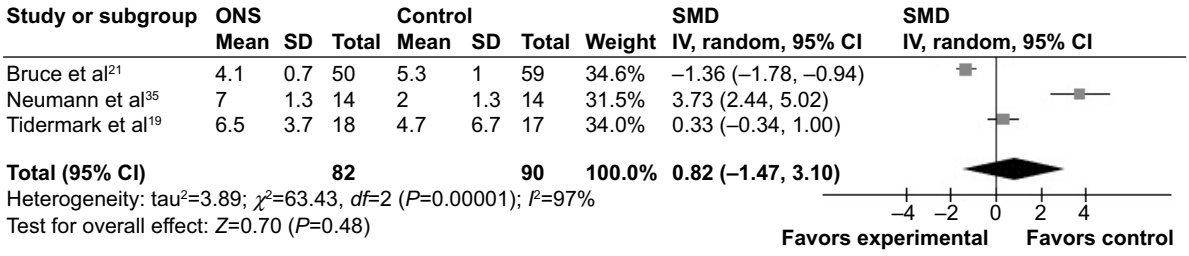

Figure 7 Forest plot for changes in serum albumin.
Notes: A random effects model was adopted. This forest plot indicates that there was no statistical improvement in change in serum albumin levels between the ONS intervention group and the control (SMD: 0.82 [95% CI: –1.47, 3.10]; *P*=0.48). Heterogeneity: I^2=97%; *P*<0.00001.
Abbreviations: CI, confidence interval; *df*, degrees of freedom; IV, intravenous; ONS, oral nutritional supplementation; SD, standard deviation; SMD, standard mean difference.

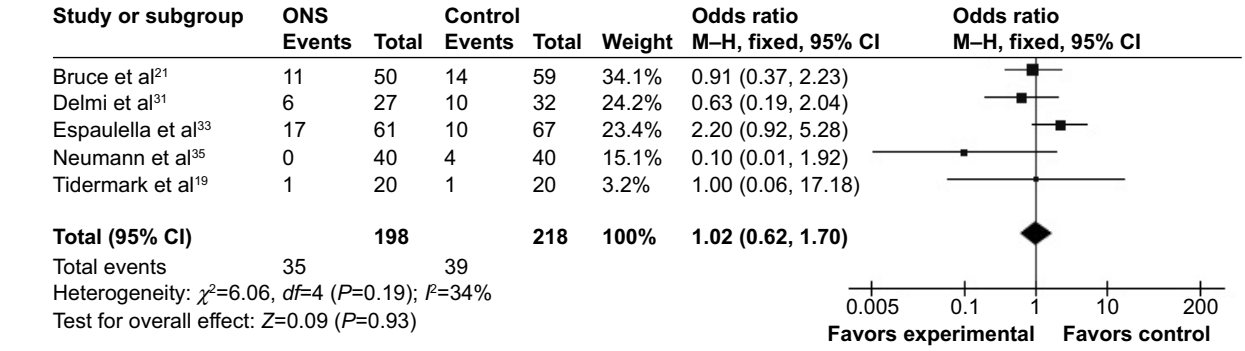

Figure 8 Forest plot for mortality.
Notes: This forest plot shows the odds ratios of mortality. The combined data indicate that there was no statistically significant difference in mortality rates between the ONS intervention group and the control (OR =1.02 [95% CI: 0.62; 1.70]; *P*=0.93). Heterogeneity: I^2=34%; *P*=0.19.
Abbreviations: CI, confidence interval; *df*, degrees of freedom; ONS, oral nutritional supplementation; M–H, Mantel–Haenszel.

showed that ONS had a positive effect on wound healing. The decreased infection rates observed in the ONS group could be related to the increased serum total protein level, which would benefit the elderly patients to maintain the immunological functions.[38] ONS had a positive effect on the respiratory infection rate as well as the wound infection rate. Furthermore, high-protein and high-calorie diets have been shown to reduce the urinary tract infection rate.[39]

As an independent prognostic factor for elderly patients after hip surgery, serum albumin is an important index for assessing rehabilitation after surgery.[40] A change in serum albumin levels before and after ONS was observed in the present study. The merged data from three trials about the change in serum albumin showed no statistically significant difference (Figure 7),[19,21,35] while there was significant heterogeneity (χ^2=63.43, *df*=2 [$P<0.00001$]; I^2=97%) was found using the random effects model. Further research should aim to define whether ONS can influence the serum albumin levels.

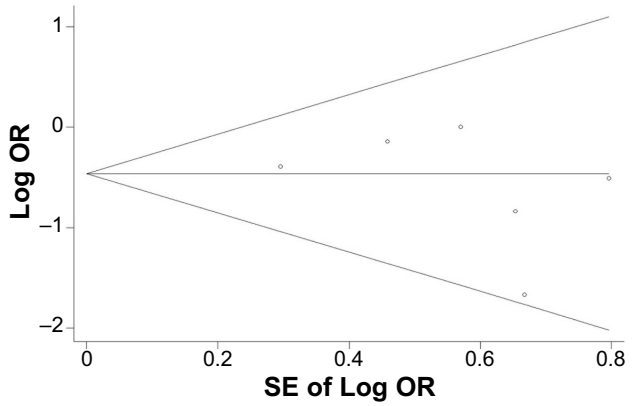

Figure 9 Begg's funnel plot for publication bias with pseudo 95% confidence limits.
Note: The presence of publication bias in studies comparing complications rates between ONS patients and controls was investigated using Begg's funnel plot.
Abbreviation: SE, standard error.

Our mortality data indicate that there were no statistical differences between the ONS group and the control group. This finding is consistent with previous studies.[20,21,33] However, more attention should be paid to one important element: unavoidable death. The differences in mortality between the ONS group and the control group were not statistically significant because inevitable deaths were not excluded. Approximately one-quarter (28%) of deaths after hip surgery in the elderly are unavoidable regardless of the perioperative care regimen.[8] The mortality rates of the two groups in the present study are both below one-quarter (ONS group: 35/198≈17.68%; control group: 39/218≈17.89%). Thus, it is inadvisable to draw the conclusion that the use of ONS in elderly patients after hip surgery has no proven effect on mortality according to Figure 8. Among the included studies, three studies had follow-up within 1 month; three within 4 months; one within 6 months; one at both 6 months and 12 months; and the other three followed-up only on the day of discharge (Table 1). Further large and high-quality randomized trials are needed to confirm these findings showing the unavoidable deaths of some patients.

The main limitations of this review were the small number of available studies and the gap between the follow-up times of included studies. When the publication bias was adjusted and each study was excluded from the model once, all the significant results observed remained valid. We found no evidence of existing publication bias. Moreover, data about the types, quantities, compositions, and timing of nutritional supplementation at any stage were not reported in any of the included studies.

Conclusion

The results from this meta-analysis suggest that perioperative ONS for elderly patients after hip surgery promotes early

rehabilitation with reduced complications and decreased infection rate. Because of the high heterogeneity, it is unclear whether perioperative ONS has an effect on increasing serum albumin levels or reducing mortality. More high-quality investigations are needed for further detailed study.

Acknowledgment

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Disclosure

The authors report no conflicts of interest in this work.

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