Author's response to reviews

Title: A Pilot Randomized Controlled Trial to Improve Geriatric Frailty

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Author's response to reviews: see over
Dear Editor:

September 3, 2012

Thank you for further comments on our manuscript. We appreciate the constructive opinions and have made appropriate revisions of the manuscript. We therefore resubmit the latest revision for your consideration of publication in BMC Geriatrics.

The manuscript is an original research that has not been published and is not under consideration elsewhere.

Thank you again for your patience, and we are looking forward to your favorable response.

Sincerely yours,

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Response to Editor Comments

You have answered to the second reviewer that GEE were used to study the 12 month course of frailty status but you show an effect only at the 3-month assessment. What was the interest of GEE in this case? I am not sure to have understood your results. If the frailty status improved at 3 month, does the lack of improvement at 12 month mean a regression to worse frailty status or not? Is it an early improvement followed by a period back to "natural" evolution? I think that few words to precise it in the results and to comment this question in the discussion are useful and if it is needed in the conclusion of the abstract.

Response: Thanks for your comment. GEE is just a statistical method to deal with longitudinal data when outcomes were measured at multiple times. Since the intervention only lasted for 3 months, it is reasonable to expect that the effects would gradually diminish without continuous reinforcement at same intensity. From our Figure 2, for EN group subjects, the improvements rate was 45% at 3 month. It decreased to 42% at 6 months, and 40% at 12 month. At the same time, the improvement rates in the non-EN groups stay roughly the same, therefore the between group differences became non-significant. We have revised our Results, Discussion, and Abstract as follows:

Results: page 15 Primary Outcomes (Figure 2) and Transition of Frailty Status (Table 3) section:

The improvement rates were highest at the end of intervention (3-month) for EN (45%) and PST (44%) groups. Afterwards, there were gradual declines of the improvement rates at 6 (42% EN group, 35% PST group) and 12 (40%, EN group, 35% PST group) months. On the other hands, the improvement rates of the non-EN, or non-PST group subjects were stable around 30%. Therefore, only the 3-month differences between EN and non-EN group (45% vs 27% p=0.008) was significant after adjusting the effect of PST and other potential confounders (Figure 2).

Discussion: In page 20 second paragraph we added

Some observational studies suggested that frailty is a dynamic process and natural transitions to better status may occur without interventions. During the intervention period, our degrees of improvement in frailty status were significantly higher than the natural improvement rates reported from observational studies. On the other hand, the improvement rates during the follow up periods were similar to other studies. It was encouraging that frailty status could be reversed with proper interventions. However, the effects might not last long when intensive interventions were discontinued.
The abstract section should be corrected according to the first remark of the 1st reviewer concerning the CHS_PCF criteria (excluding 1 and 2 and 7 and not only 1?). The sentence "Assessments were performed etc.." is not very useful here but the analysis plan (GEE for the 12-month or other) much more. You should delete the end of the sentence concerning control group because you have no data to support the statement that educational booklet was at the origin of the improvements seen in the control group.

Response: Thanks you, we agree with your comments. We therefore have revised the abstract according to your suggestions as follow:

BACKGROUND: Few randomized controlled trials (RCTs) report interventions targeting improvement of frailty status as an outcome.

METHODS: This RCT enrolled 117 older adults (65–79 years of age) in Toufen, Taiwan who scored 3–6 on The Chinese Canadian Study of Health and Aging Clinical Frailty Scale Telephone Version and then score ≥1 on the Cardiovascular Health Study Phenotypic Classification of Frailty (CHS_PCF). With a two by two factorial design, subjects were randomly assigned to interventions (Exercise and nutrition, EN, n=55 or problem solving therapy, PST, n=57) or controls (non-EN, n=62 or non-PST, n=60). Educational booklets were provided to all. EN group subjects received nutrition consultation and a thrice-weekly exercise-training program while PST group subjects received 6 sessions in 3 month. Subjects were followed at 3, 6, and 12 months. (Assessment part deleted) Primary outcome was improvement of the CHS_PCF by at least one category (from pre-frail to robust, or from frail to pre-frail or robust) from baseline assessments. One hundred and one completed final assessments.

Intention-to-treat analysis with the generalized estimating equation model was applied with adjustment for time and treatment-by-time interactions.

RESULTS: Mean age was 71.4 ± 3.7 years, with 59% females. Baseline characteristic were generally comparable between groups. EN group subjects had a higher improvement rate on the primary outcome than non-EN group subjects (45% vs 27%, adjusted p=0.008) at 3 months, but not 6 or 12 months. They also had more increase of serum 25(OH) vitamin D level (4.9 ± 7.7 vs 1.2 ± 5.4, p=0.006) and lower percentage of osteopenia (74% vs 89% p=0.042) at 12 months. PST group subjects had better improvement (2.7 ± 6.1 vs 0.2 ± 6.7, p=0.035, 6-month) and less deterioration (-3.5 ± 9.7 vs -7.1 ± 8.7, p=0.036, 12-month) of dominant leg extension power than non-PST subjects. Some secondary outcomes were also improved in control groups (booklet part deleted) (non-EN or non-PST). No adverse effects were reported.
CONCLUSIONS: The three-month EN intervention resulted in short-term (3-month) frailty status improvement and long-term effect on bone mineral density and serum vitamin D (12-month) among Taiwanese community-dwelling elders. The effect of PST was less pronounce.