Author’s response to reviews

Title: Quality of life after the initiation of dialysis or maximal conservative management in elderly patients: A longitudinal analysis of the Geriatric assessment in OLder patients starting Dialysis (GOLD) Study

Authors:

Ismay van Loon (I.vanloon@dianet.nl)
Namiko Goto (n.a.goto@umcutrecht.nl)
Franciscus Boereboom (f.boereboom@dianet.nl)
Marianne Verhaar (m.c.verhaar@umcutrecht.nl)
Michiel Bots (m.l.bots@umcutrecht.nl)
Marije Hamaker (mhamaker@diakhuis.nl)

Version: 2 Date: 08 Oct 2018

Author’s response to reviews:

Dear Editor,

We want to thank you for the opportunity of resubmitting our manuscript to BMC Nephrology after major revisions. We appreciate the time the reviewers took to comment on our manuscript. We discussed all items together and revised the manuscript. We addressed these comments below one by one. We think the comment of the reviewers contributed to the improvement of the manuscript.

We hope that the revised version of the manuscript is suitable for publication in your journal.

With kind regards, also on behalf of my co-authors,

Ismay van Loon

Reviewer 1.

1. We agree with the reviewer that the time point is very difficult in observational studies on the comparison between dialysis and conservative care.
Our starting point was to compare outcomes (geriatric assessment and QoL) at the start of dialysis with 6 months follow-up data (primary analysis). In addition, we wanted to compare this with the trajectory of conservative patients. To make a reasonable comparison we choose to compare patients who made the decision for conservative therapy in the pre-dialysis clinic after shared decision-making, but only if GRF had dropped below 15 ml/min.

When looking at the mean eGFR of conservative patients in our cohort (eGFR 11.5±4.0) it was significantly higher compared to dialysis patients 8.0±2.9. This reflects the custom to start at a lower GFR (< 10 ml/min) nowadays. However, still 20% of the dialysis patients (40/196) of the patients started at an eGFR between 10-15 ml/min/1.73m2.

Others found a relation between frailty and earlier start of dialysis, although the actual causal pathways among uremia, frailty, and earlier dialysis initiation have yet to be determined. In our cohort this was also the case: mean eGFR in frail patients (poor Fried frailty index) was 8.6 +/- 3.2 compared to fit patients 7.6 +/- 2.6, p=0.02

We agree with the reviewer that lead time bias is an important issue here. Consequently, we have included eGFR in our analysis to correct for this phenomenon as good as possible. Unfortunately, due to limited amount of allowed words, we could not add this to the text.

The primary outcome of the study was the score on a geriatric assessment and relation with poor outcome (described in another manuscript, under review at the moment). So no power analysis was performed to detect a change in quality of life. However, for the EQ-D5 we detected a significant and clinically relevant decline in the conservative group.

We’ve added to the method section:

“For the second group, patients were included < 3 months after the decision to forgo dialysis had been made after shared-decision making according local practice of the pre-dialysis clinic, and if GFR was < 15 ml/min (either estimated with CKD-EPI or measured with 24-hours urine creatinine clearance).”

2. In frail elderly patients it can be very difficult to decide who will benefit from dialysis. For patients who die or deteriorate quickly after dialysis initiation, the burden of starting dialysis did not outweigh the benefits. With the GOLD study we tried to identify factors associated with poor outcome in order to identify patients who might benefit more from conservative care. Only few data are available on the trajectory of QoL after dialysis initiation and after the choice for conservative care. Although we agree with the reviewer that more research is needed to capture a better picture of the trajectory of QoL of elderly with ESKD, including a longer follow-up period, we think the short FU period is still relevant for the follow-up reasons:

1) Although the transition to dialysis can have a large impact on elderly patients, our results show that in two-thirds of elderly patients QoL improves afterwards. This is relevant information to share. (We’ve added this to the discussion).
2) Short-term mortality is high in the elderly ESKD population, especially in the conservative group, were 1 out of 7 died within 6 months. Thus, measuring the short-term trajectory of QoL is also relevant in the ESKD conservative population. In addition, we showed that hospitalizations in the first six months occurred in twice as many dialysis patients compared to conservative patients.

Reviewer 2.

1. Patients with a terminal condition and limited life expectancy do not resemble the domain of our study. Our population of interest is patients with end-stage kidney disease who either chose conservative care or dialysis. It can be a difficult choice for patients and knowledge on quality of life on either modality could help with the decision. This is explained in the introduction.

For patients with a terminal disease there is no choice but conservative care in many countries (including The Netherlands) as they won’t benefit from dialysis and their quality of life will be much worse as compared with non-terminal ill ESKD patients.

2. There is general consensus that a geriatric assessment is the best systematic approach for the identification of frailty in clinical practice. The geriatric assessment is a multidimensional approach to evaluate the health status of elderly patients regarding somatic, functional, and psychosocial domains in a systematic and evidenced-based way.

“Frailty was assessed with a geriatric assessment, generally considered the best systematic approach for identification of frailty.”

3. The EuroQol-5D-3L consists of two parts the Index and VAS. We explained this more clearly in the text. The time points are noted under Follow-up.

4. First, quality of life as measured with the EQ-D5 declines with age and in the general population scores on mobility, self-care and activities are relevantly lower in 80+ patients. Second, the decision to forgo dialysis changes with the age of the patients. Some physicians consider decision-making more difficult with ascending age (40%), whereas others (30%) considered it less difficult when patients get older. Third, survival on dialysis was found not significantly longer in patients choosing conservative care vs. dialysis, while there is a survival benefit in younger patients. Based on these differences we found it relevant to perform a subgroup analysis for the 80+ group. Due to limited amount of words we could not add this background information to the text.
5. This was done to correct for lead time bias and because some of the EQ-D5 scores (mobility, self-care, usual activities) decrease with increasing age. 

6. The difficulty with describing QoL in dialysis patients is attrition due to death (probably the most frail patients with consequently the lowest QoL) and kidney transplantation (probably the fittest patients with the highest QoL). We chose to do include all patients in an intention to treat analysis. In our opinion we would introduce a big selection bias if we analyzed only QoL of the patient who would still be alive at follow-up. This is the reason we choose a composite endpoint decline of QoL or death. Only a small percentage of the patients (15% and 8% of conservative and dialysis patients resp.) died.

Results:

1. We’ve added the univariate outcome of the domain mobility. Anxiety/depression was added because it was statistically different between the two groups when adjusted for age and eGFR.

2. See methods question 5.

3. We agree this is not statistically significant and changed the results accordingly.

4. Done as suggested.

5. In the methods we describe: For the first group, eligible patients were included between 3 weeks before and 2 weeks after the first dialysis session.

   In the results “Four dialysis patients were excluded from the follow-up analyses, as they did not meet the inclusion criteria regarding the interval between time of inclusion and start of dialysis.”

   We’ve added in the methods: “If dialysis would start >3 week after the geriatric assessment, patients were excluded from the follow-up”.

6. These variables were included because of clinical relevance (age and comorbidity burden) and to adjust for lead time bias (eGFR).

7. We rewrote this paragraph:
“After six months, anxiety/depression decreased in the dialysis group from 31% to 21% (p<0.01), while in the conservative group this remained stable (24%, Table 2); the other domains did not change significantly. Overall, more impairment was found in the conservative group at follow-up. Mobility impairment (78% conservative vs. 55% dialysis, p < 0.01), self-care impairment (41% vs. 24%, p<0.01) and pain/discomfort (66% vs. 44%, p<0.01) were more prevalent in the conservative group., However, when adjusted for age and eGFR no significant differences in EQ-D5 domains were found between the two groups (data not shown).”

8. Leaving the patients who received a kidney transplant out the analysis, would also introduce bias. We chose to include all patients (like an intention to treat analysis). In this way the results would be better comparable to the clinical practice.

9. At six months: 29 hospitalizations occurred in the conservative group and 153 in the dialysis group. We rewrote the paragraph on hospitalizations.

“Hospitalizations (≥1 in six months) occurred in 50% of dialysis patients and in 24% of conservative patients (p<0.01). Among hospitalized patients, median number of admissions was 1 [range 1-5] for dialysis patients and 1 [range 1-4] for conservative patients (p=0.27). Median number of admission days was 7 [interquartile range, IQR, 3-15] for dialysis patients and 4 [IQR 2-12] for conservative patients (p=0.22). “

Discussion:

1. We’ve changed the sentence:

“First, EQ-D5 Index was higher in patients starting dialysis, with less pain/discomfort compared to patients choosing conservative care.”

2. We think in a study on elderly patients, it is relevant to know how healthy older patients perform. As we don’t have data on a comparable cohort (age, frailty, comorbidity burden) of patients with another chronic illness, we are not able to perform a reliable comparison with such a cohort.

3. The reviewer is correct, no. of hospitalizations and % of patients with hospitalizations got mixed up. We still think it is very relevant that more dialysis patients were hospitalized as compared to conservative patients. We changed the sentences on this topic:

“Third, significantly more dialysis patients were hospitalized at least once compared to conservative patients, despite the conservative patients being older. (removed: “hospitalizations occurred” [significantly more]).”
“In our study, half of the dialysis patients were hospitalized compared to one out of four of the conservative patients. (removed: “hospitalization was twice as high….”)”

References


