CORRESPONDENCE

Effect of Hemodiafiltration or Hemodialysis on Mortality in Kidney Failure

TO THE EDITOR: We have been interested in the use of hemodiafiltration for more than 40 years, and we reported on the results of an early longitudinal study on hemodiafiltration.[1] The results of the Dialysis Outcomes and Practice Patterns Study[2] suggested that high convection volumes (>17 liters per session) provided a survival benefit; however, a later study did not support those findings.[3] In a randomized trial conducted in Catalonia,[4] a survival benefit was observed when the convection volume exceeded 18 liters per session.

Now, in the CONVINCE trial, the results of which are reported by Blankestijn et al. (Aug. 24 issue),[5] the use of high-dose hemodiafiltration has been found to result in a lower risk of death from any cause than conventional high-flux hemodialysis in a group of patients that was deemed to be candidates for a convection volume of at least 23 liters per session. Indeed, investigators observed a lower incidence of infection-related death, including from Covid-19 (the trial was conducted during the pandemic), with high-dose hemodiafiltration than with conventional high-flux hemodialysis and a similar risk of death from cardiovascular causes in the two groups. The trial was well-performed, and the results were eagerly awaited. However, although the trial was "pragmatic" in design, the selected group of patients is far from representative of the persons attending dialysis clinics. Therefore, by concluding that the survival benefits are applicable to "patients with kidney failure resulting in kidney-replacement therapy," the investigators involuntarily overstate their findings through generalization.

Àngel Argilés, M.D., Ph.D.

Néphrologie Dialyse Saint Guilhem
Sète, France

Alain Ficheux, B.Sc.
Flore Duranton, Ph.D.

RD–Néphrologie
Montpellier, France
duranton@rd-n.org

No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Blankestijn et al. report the results of the CONVINCE trial, which showed a 23% lower risk of death from any cause with high-dose hemodiafiltration than with high-flux hemodialysis. Unfortunately, residual urinary output was recorded in only 12% of the patients. Thus, the subgroup analysis of the effect of this variable on mortality cannot be interpreted with confidence. Indeed, the authors present the results according to urinary output categories of less than 1000 ml per day or 1000 ml or higher per day, whereas the protocol included a third category (<200 ml per day). The lack of information regarding residual urinary output is unlikely to be missing randomly in medical files.

Most of the patients in the CONVINCE trial (median dialysis vintage, approximately 33 months) probably had little urinary output.[1] This is a critical point — a residual urinary output of 200 to 499 ml per day is associated with better survival than an output of less than 200 ml per day.[1] Post hoc analyses of the Hemodialysis (HEMO) study[2] showed that high-flux hemodialysis, as compared with low-flux hemodialysis, conferred a survival benefit in patients with a dialysis vintage of more than 3.7 years. Could the authors provide the dialysis vintage, as a possible surro-

gate for residual urinary output, in patients with a daily residual urinary output of less than 200 ml, in those with a urinary output between 200 and 1000 ml, and in those with a urinary output of more than 1000 ml, along with the number of patients whose urinary output data were missing?

Laura Labriola, M.D.
Guillaume Fernandes, M.D.
Michel Jadoul, M.D.

Cliniques Universitaires Saint-Luc
Brussels, Belgium
laura.labriola@saintluc.uclouvain.be

Dr. Jadoul reports being cochairperson of Kidney Disease Improving Global Outcomes (KDIGO) since January 2019. No other potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: As important studies do, the CONVINCE trial poses questions. Individualized care is increasingly integrated in dialysis prescriptions. Thus, should we look for the single best treatment or contextualize the CONVINCE results to fitter patients? The advantages reported in the trial are greater in younger and healthier patients; however, the conclusions are not nuanced. Would it be unethical to treat older and fragile patients with incremental and personalized strategies?[1] Economic and empowerment considerations suggest choosing out-of-hospital dialysis whenever possible.[2] However, high-dose hemodiafiltration is not systematically available and is even banned in out-of-hospital settings in some countries (France, for example). Would it be unethical to prescribe home or out-of-hospital hemodialysis for young patients? In a schizophrenic balance between personalization and standardization of dialysis schedules, between shorter (or no) hospitalization and high-intensity care, we hope that this trial will convince health care authorities to invest in updating out-of-hospital dialysis networks (and where needed, to modify the relevant laws), without setting the clock back with respect to the personalization of hemodialysis, which is not just a schedule but a global approach to patients' needs.[3,4]

Giorgina B. Piccoli, M.D.
Massimo Torreggiani, M.D., Ph.D.

Centre Hospitalier Le Mans
Le Mans, France
gbpiccoli@yahoo.it

Hafedh Fessi, M.D.

Hôpital Tenon
Paris, France

No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: We certainly agree with the comment by Argilés and colleagues that the inclusion criteria of the CONVINCE trial resulted in a certain degree of patient selection, as we indicated in the Discussion section of the article. In a previous report on the combined data set of the four earlier European trials, we constructed an algorithm that estimates which patients would be the most likely to benefit from hemodiafiltration on the basis of demographic and clinical characteristics.[1] The current article already contains practical suggestions regarding the type of patient that would be most likely to benefit.

We appreciate the comment by Labriola and colleagues. Indeed, residual urinary output is potentially relevant in an analysis such as ours. Furthermore, it is not impossible that the loss of residual urinary output over time could differ between the two groups. Such a difference, if present, could be of relevance in explaining the overall beneficial effect. Because CONVINCE was a pragmatic trial that did not interfere with routine clinical practice, information regarding residual renal function was indeed limited at baseline and was not collected during follow-up. Therefore, although Labriola and colleagues have a relevant suggestion, we are unfortunately unable to address it. Dialysis vintage was analyzed separately (Fig. 2B in the article).

Piccoli and colleagues point toward personal-

ized treatment. We are currently updating the previous findings of our study in which we constructed an algorithm that estimates the type of patient that would be most likely to benefit from hemodiafiltration.[1] This information may help in the process of shared decision making. Cost effectiveness is also currently being addressed with the use of the CONVINCE data. The next step is for guideline committees, regulatory authorities, and other relevant stakeholders to determine the place of hemodiafiltration on the basis of the currently available evidence. The interesting ethical issues raised are beyond the scope of the article.

Peter J. Blankestijn, M.D.
Michiel L. Bots, M.D.

University Medical Center Utrecht
Utrecht, the Netherlands
p.j.blankestijn@umcutrecht.nl

Since publication of the article, the authors report no further potential conflict of interest.

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