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Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

New England Journal *of Medicine*

October 22, 2009

Background

- Some of the subtler points regarding the optimal strategy in RRT in critical illness remain unclear.
- In a study of 425 patients, Ronco et al[1]. reported a decrease in mortality from 59 to 43% when the prescribed effluent flow was increased from 20ml/ kilogram/hour to 35 or 45ml/kilogram/hour.
- Saudan et al.[2] found similarly in 206 patients.
- Other single centre RCTs[3,4] have failed to replicate this.

Study Design

- Prospective, randomized, parallel-group trial conducted in 35 ICUs across Australia.
- Patients requiring RRT randomised to continuous haemodiafiltration with effluent flow either 25ml/kg/hr (low intensity) vs. 40ml/kg/hr (high intensity).
- Primary endpoint was survival at 90 days.

Eligibility

- Critically ill (as defined by clinician)
- 18 years of age or older
- Have acute kidney injury
- Deemed by the treating clinician to require RRT.

- Must also meet at least one of the following criteria:
  - oliguria (urine output <100 ml in a 6-hour period) unresponsive to fluid
  - a serum potassium >6.5 mmol per litre
  - severe acidemia (pH <7.2)
  - urea >25 mmol per litre
  - serum creatinine >300 µmol per litre
  - presence of clinically significant organ edema (e.g.,pulmonary edema).

- Excluded patients receiving RRT for end stage renal disease or those who had received it earlier in the same hospital admission.

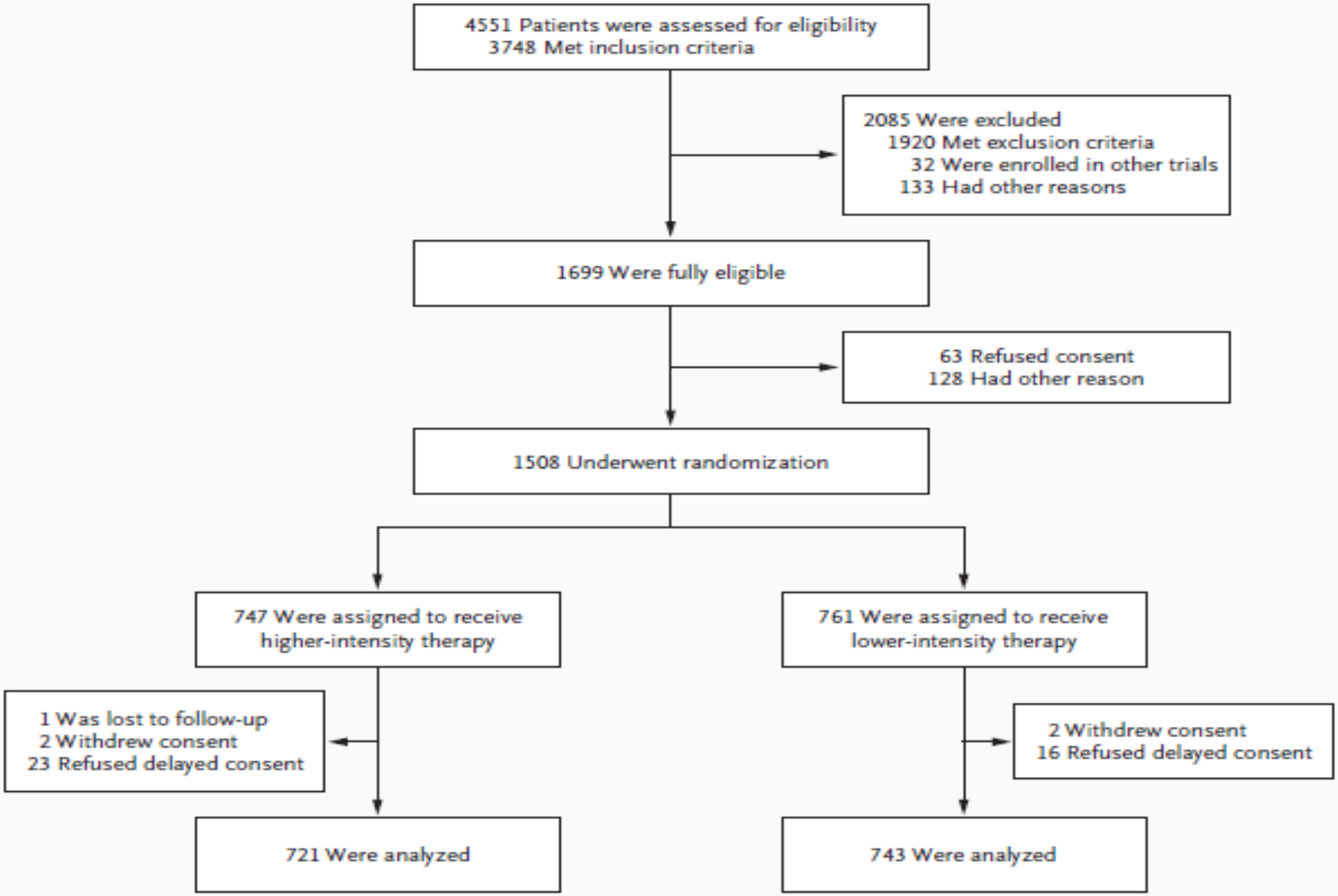

Figure 1. Numbers of Patients Enrolled in the Study, Randomly Assigned to a Treatment Group, and Included in the Analysis.

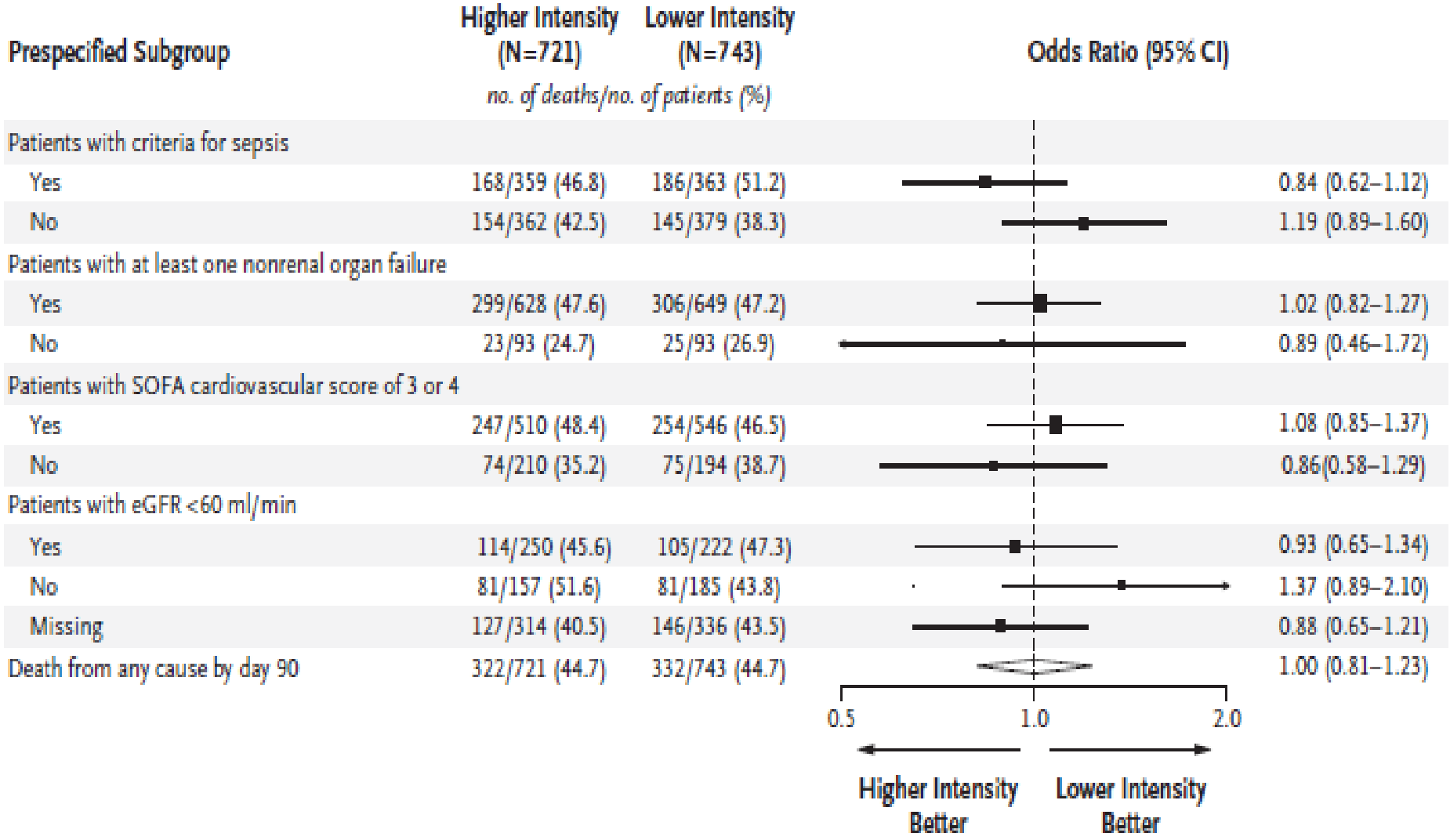

Figure 3. Mortality in the Prespecified Subgroups and among All Patients.

Odds ratios and 95% confidence intervals are shown for deaths in the four prespecified subgroups for both treatment pairs and for death from any cause by day 90 for all patients. CI denotes confidence interval, eGFR estimated glomerular filtration rate, and SOFA Sequential Organ Failure Assessment (range of scores, 0 to 4). Larger squares represent greater numbers of patients.

Table 3. Primary and Secondary Outcomes.*

Outcome	Higher-Intensity CRRT	Lower-Intensity CRRT	Odds Ratio	P Value†
Death — no./total no. (%)				
By day 90	322/721 (44.7)	332/743 (44.7)	1.00 (0.81–1.23)	0.99
By day 28	278/722 (38.5)	274/743 (36.9)	1.07 (0.87–1.32)	0.52
Place of death — no./total no. (%)				
ICU	251/722 (34.8)	254/743 (34.2)	1.026 (0.827–1.273)	0.81
Hospital ward	68/722 (9.4)	76/743 (10.2)	0.913 (0.647–1.288)	0.60
Outside hospital, after discharge	3/722 (0.4)	2/743 (0.3)	1.546 (0.258–9.279)	0.63
RRT dependence among survivors				
At day 28	64/443 (14.4)	57/469 (12.2)	1.22 (0.83–1.79)	0.31
At day 90	27/399 (6.8)	18/411 (4.4)	1.59 (0.86–2.92)	0.14
No. of days of RRT, from randomization to day 90	13.0±20.8	11.5±18.0	—	0.14
No. of days in ICU	11.8±14.1	11.8±14.2	—	0.95
No. of days in hospital	26±25.8	25.7±24.7	—	0.79
No. of days of mechanical ventilation	7.3±5	7.4±5	—	0.79
No. of nonrenal organ failures — no./total no. (%)‡				
0	344/722 (47.6)	343/743 (46.2)	—	0.57
1	254/722 (35.2)	263/743 (35.4)	—	0.93
2	100/722 (13.9)	109/743 (14.7)	—	0.65
3	23/722 (3.2)	25/743 (3.4)	—	0.85
4	1/722 (0.1)	3/743 (0.4)		0.33

Paper strengths

- Multicentre prospective RCT answering a relevant clinical question.
- Well powered
- Predefined subgroups and methodology published before results
- Only one primary endpoint

Paper weaknesses

- Clinician discretion regarding what constitutes “critically ill” and “requires RRT” may be regarded by some as not being well defined.
- Multiple secondary endpoints (but all negative barring more hypophosphataemia in high intensity group, 65% vs. 54%).
- Inability to effectively blind observers – note treatment limitations same in both groups.

Questions