



Sanquin

Blood and Beyond

Anemie en transfusies bij cardiochirurgie

Sanquinavond, 4 Maart 2015

Leo van de Watering

Sanquin Bloedvoorziening Nederland

Divisie Research, CCTR

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Wie is de boosdoener?

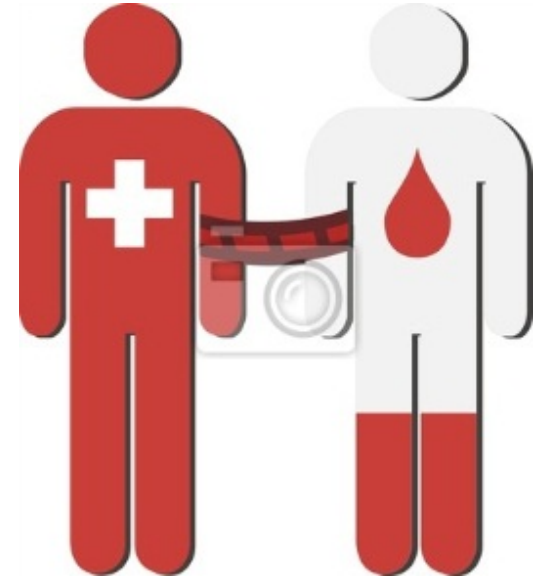
In de literatuur: Transfusies → Slechtere prognose

Anemie → Slechtere prognose

“Indicatie Bias”

Wel/niet transfunderen bij anemie:

Randomiseren: Triggers

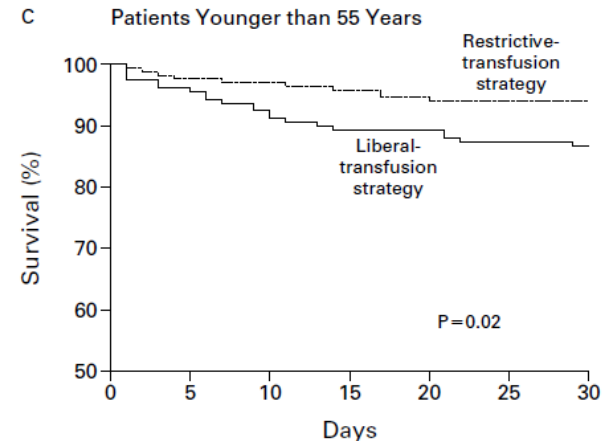
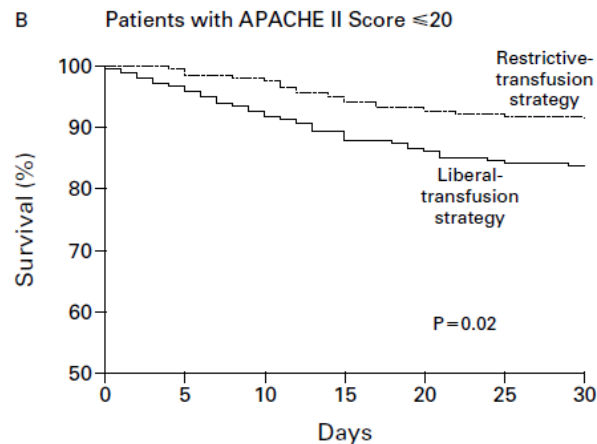
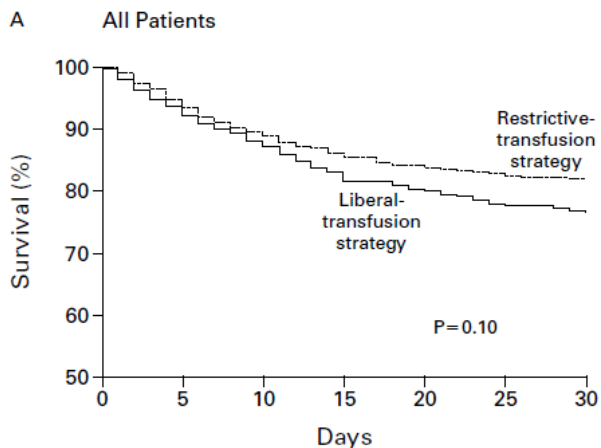


Trigger studies

A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

PAUL C. HÉBERT, M.D., GEORGE WELLS, PH.D., MORRIS A. BLAJCHMAN, M.D., JOHN MARSHALL, M.D., CLAUDIO MARTIN, M.D., GIUSEPPE PAGLIARELLO, M.D., MARTIN TWEEDDALE, M.D., PH.D., IRWIN SCHWEITZER, M.Sc., ELIZABETH YETISIR, M.Sc., AND THE TRANSFUSION REQUIREMENTS IN CRITICAL CARE INVESTIGATORS FOR THE CANADIAN CRITICAL CARE TRIALS GROUP*

Restrictive: 7(-9) g/dL versus Liberal: 10(-12) g/dL



(N Engl J Med 1999;340:409-17.)

Trigger studies

Transfusion Requirements in Surgical Oncology Patients

A Prospective, Randomized Controlled Trial

Results: A total of 198 patients were included as follows: 101 in the restrictive group and 97 in the liberal group. The primary composite endpoint occurred in 19.6% (95% CI, 12.9 to 28.6%) of patients in the liberal-strategy group and in 35.6% (27.0 to 45.4%) of patients in the restrictive-strategy group ($P = 0.012$). Compared with the restrictive strategy, the liberal transfusion strategy was associated with an absolute risk reduction for the composite outcome of 16% (3.8 to 28.2%) and a number needed to treat of 6.2 (3.5 to 26.5).

Conclusion: A liberal erythrocyte transfusion strategy with a hemoglobin trigger of 9 g/dl was associated with fewer major postoperative complications in patients having major cancer surgery compared with a restrictive strategy. (ANESTHESIOLOGY 2015; 122:29-38)

De (liberale) trigger van **9 g/dl** was geassocieerd met **MINDER** post-operatieve complicaties

Alle triggers apart in RCT's testen in alle patient groepen?

Wat is slechter: anemie of transfusie?

In de literatuur: **Transfusies → Slechtere prognose**

Anemie → Slechtere prognose

“Bias by indication”

Wel/niet transfusies bij anemie:

Randomiseren: *Triggers*

Patients keuze: Jehova's getuigen

Amphia Zh, Breda

Amphia Cardiac Surgery Blood Management Study

1997 – 2013

23860 patiënten

Referentiecentrum voor Jehova getuigen

Ernstige eindpunten

1. Myocard infarct
2. Nierfunctie vervangende therapie
3. CVA
4. In ziekenhuis mortaliteit
5. Gecombineerd eindpunt (1 – 4?)

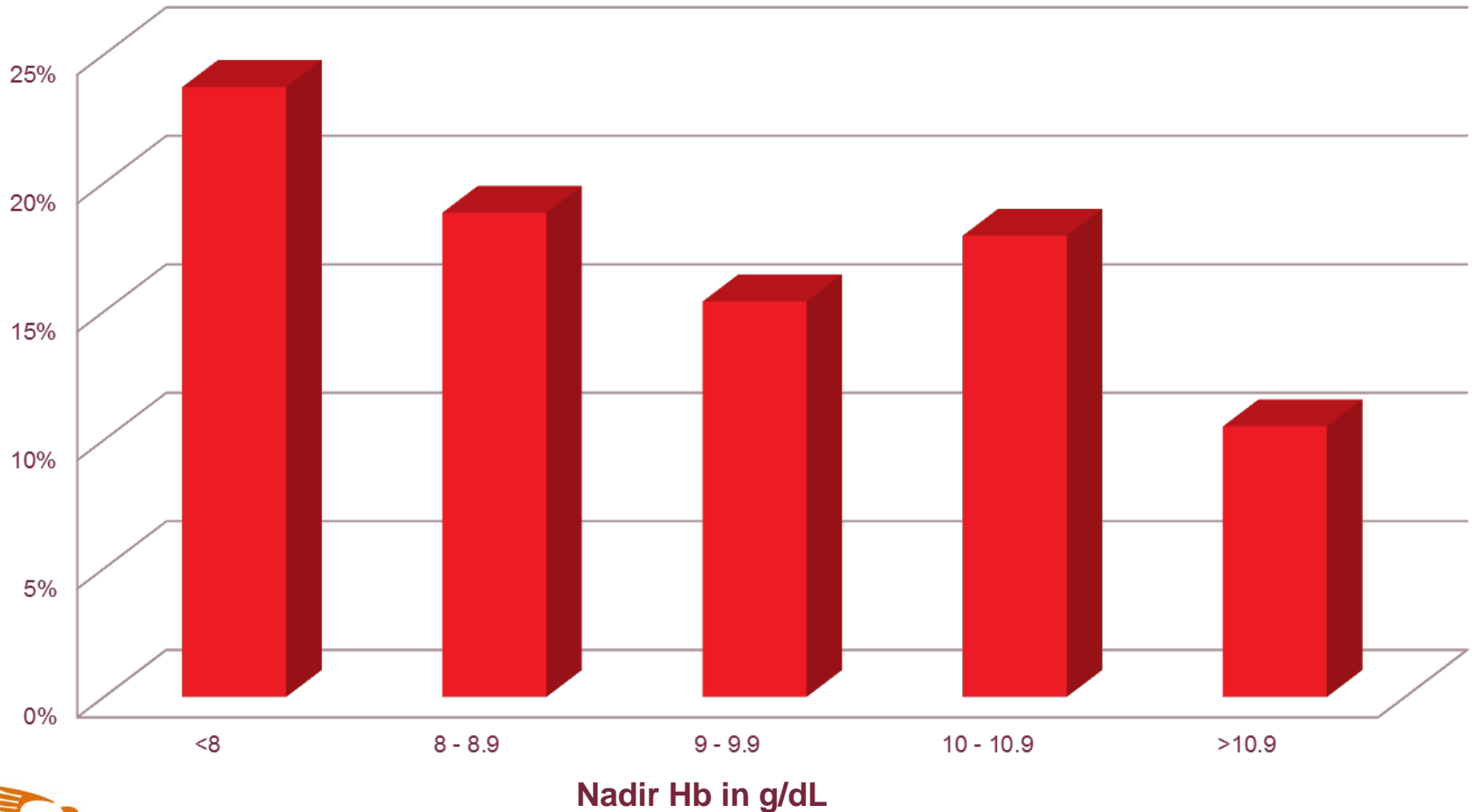
3 Analyses

1) Effect van Anemie
Jehova getuigen & niet-JG (0 RBC)

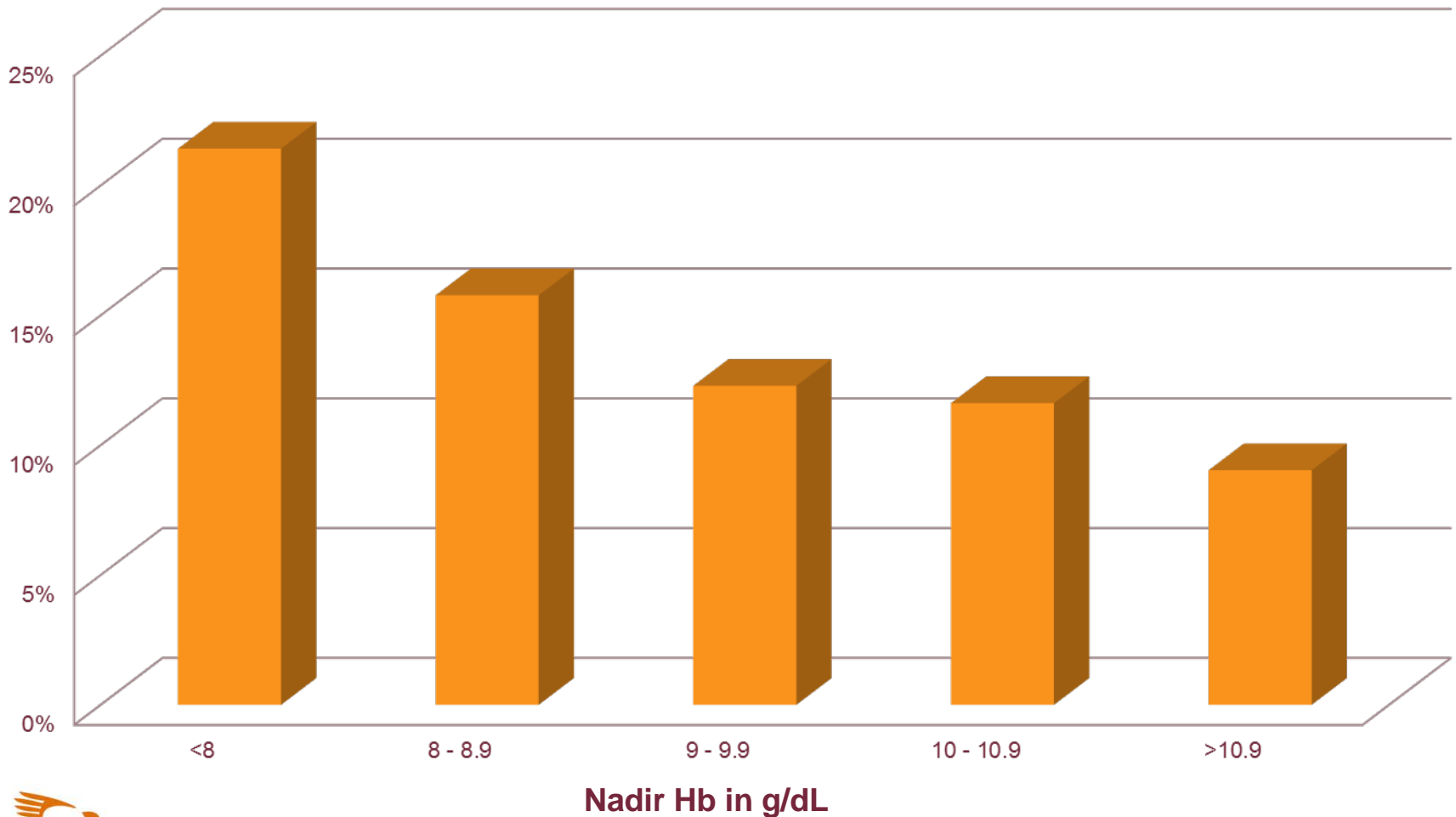
2) Effect van transfusie-I
Jehova getuigen vs niet-JG (1 RBC)

3) Effect van transfusie-II
niet-JG (0 RBC) vs niet-JG (1 RBC)

Gecombineerd eindpunt



Gecombineerd eindpunt



Studies bij Jehova getuigen

CAVE: Selectie Bias

Ingrepen: Grotere, zwaardere ingrepen worden relatief minder vaak bij Jehova getuigen verricht.



→ Propensity scores: ASA IV; Co-morbiditeit; medicatie

Propensity score-1

voorspel de kans op JG: met behulp van 37 variabelen:

age (as a continuous variable), sex, weight, year of surgery, previous cardiac surgery, current smoking, pre-operative Hb (g/dL), hypercholesterolemia (> 6.4 mmol/l), creatinine level (as continuous variable), vascular disease (defined as having previous vascular surgery and/or intermittent claudication or awaiting any vascular intervention), left ventricle hypertrophy (diagnosed by pre-operative echocardiography), atrial fibrillation, hypertension (diagnosis retrieved from patients history and/or treatment with antihypertensive drug therapy), COPD (diagnosis retrieved from patients history and active treatment with bronchodilators and/or corticosteroids), diabetes (defined as receiving any anti-diabetic drug therapy), number of coronary arteries affected, >50% LAD occlusion, pre-operative myocardial infarction (as diagnosed by the referring cardiologist), pre-operative ejection fraction; good = >50%, moderate = 25-50%, severe = < 25% (diagnosed by either pre-operative angiography, scintigraphy or echocardiography) , either aortic, mitral or tricuspid valve disease (defined as stenosis, insufficiency or both), NYHA class IV, cardiovascular insufficiency (defined as: NYHA class IV and/or preoperative nitrate intravenously (iv.) and/or heparin iv. and/or intra-aortic balloon pump (IABP)), respiratory failure (defined as the need for pre-operative mechanical ventilation), aspirin use, clopidogrel or ticagrelor use, use of anti-coagulant drugs (heparin, low molecular weight heparin (LMWH), coumarines or a combination), preoperative treatment with the following drugs; calcium antagonist, beta blockers, nitrate ACE/AT inhibitor or inotropic agents, cardiopulmonary resuscitation (CPR) 24h before surgery, emergency surgery, type of surgery (CABG, CABG + valve surgery, CABG + other, valve surgery or other) and EuroSCORE I.

Propensity score-2

Zijn er JG met een laagste **Hb <8 g/dL** ($\approx 4,9$ mmol/L)
of een peroperatieve **Hb-daling van $\geq 50\%$** ? → 66

Voor 61 van deze 66 JG patienten kon een, met 1
RBC, getransfundeerde niet-JG patient gevonden
worden met een vergelijkbare propensity score
(nearest neighbour)

JG versus 1 RBC

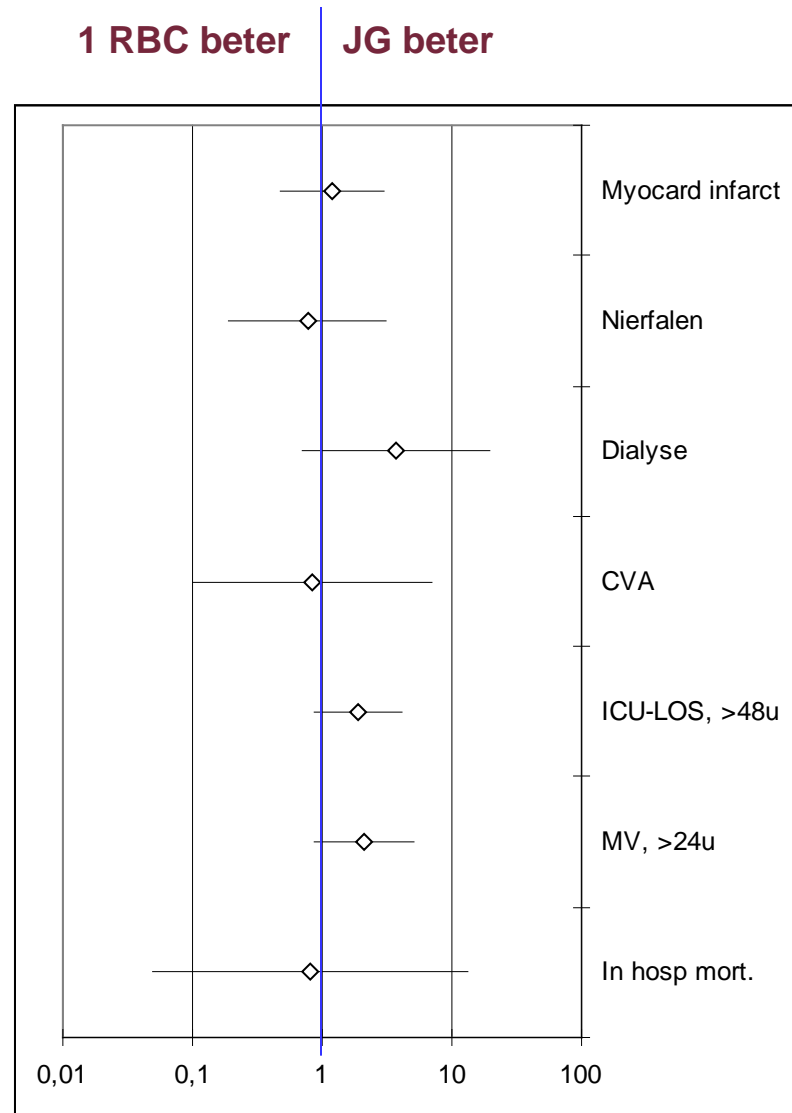
Table 2: Postoperative Outcomes in patients with an intra-operative nadir Hb < 8 g/dL and or an intra-operative Hb decrease \geq 50%

| | Jehovah's Witnesses (N =61) | Transfused patients (1unit) (N =61) | Crude OR (95% CI) | aOR* (95% CI) |
|-----------------------------------------------------|--------------------------------|-------------------------------------------|----------------------|------------------|
| - Myocardial infarction, N (%) | 12(19.7) | 13(21.3) | 1.11(0.46-2.67) | 1.18(0.47-2.96) |
| - Acute kidney injury, N (%) | 5(8.2) | 6(9.8) | 1.22(0.35-4.24) | 0.77(0.19-3.06) |
| - CVVH de novo, N (%) | 2(3.3) | 6(9.8) | 3.22(0.62-16.62) | 3.68(0.69-19.73) |
| - Stroke, N (%) | 2(3.3) | 2(3.3) | 1.00(0.14-7.34) | 0.83(0.10-7.03) |
| - ICU length of stay (hours), median (IQR) | 24(22-58) | 48(23-91) | | |
| - ICU length of stay > 48 hours, N (%) | 22(36.1) | 30(49.2) | 1.72(0.83-3.54) | 1.89(0.88-4.06) |
| - Mechanical ventilation time (hours), median (IQR) | 11(8-22) | 17(10-30) | | |
| - Mechanical ventilation > 24 hours, N (%) | 11(18.0) | 19(31.1) | 2.06(0.88-4.80) | 2.13(0.88-5.16) |
| - In hospital mortality, N (%) | 1(1.6) | 2(3.3) | 2.03(0.18-23.0) | 0.81(0.05-13.51) |
| - Hb level at discharge (g/dL), median (IQR) | 10.8(10.4-11.3) | 10.6(10.0-10.8) | | |
| - Composite endpoint**, N (%) | 15(24.6) | 20(32.8) | 1.50(0.68-3.30) | 1.44(0.63-3.29) |

* Adjusted for: intra-operative nadir Hb (g/dL)

** Composite endpoint consisting of: Myocardial infarction, CVVH, Stroke, in hospital mortality

JG versus 1 RBC



Propensity score BT

voorspel de kans op BT: met behulp van 37 variabelen:

age (as a continuous variable), sex, weight, year of surgery, previous cardiac surgery, current smoking, pre-operative Hb (g/dL), hypercholesterolemia (> 6.4 mmol/l), creatinine level (as continuous variable), vascular disease (defined as having previous vascular surgery and/or intermittent claudication or awaiting any vascular intervention), left ventricle hypertrophy (diagnosed by pre-operative echocardiography), atrial fibrillation, hypertension (diagnosis retrieved from patients history and/or treatment with antihypertensive drug therapy), COPD (diagnosis retrieved from patients history and active treatment with bronchodilators and/or corticosteroids), diabetes (defined as receiving any anti-diabetic drug therapy), number of coronary arteries affected, >50% LAD occlusion, pre-operative myocardial infarction (as diagnosed by the referring cardiologist), pre-operative ejection fraction; good = >50%, moderate = 25-50%, severe = < 25% (diagnosed by either pre-operative angiography, scintigraphy or echocardiography), either aortic, mitral or tricuspid valve disease (defined as stenosis, insufficiency or both), NYHA class IV, cardiovascular insufficiency (defined as: NYHA class IV and/or preoperative nitrate intravenously (iv.) and/or heparin iv. and/or intra-aortic balloon pump (IABP)), respiratory failure (defined as the need for pre-operative mechanical ventilation), aspirin use, clopidogrel or ticagrelor use, use of anti-coagulant drugs (heparin, low molecular weight heparin (LMWH), coumarines or a combination), preoperative treatment with the following drugs; calcium antagonist, beta blockers, nitrate ACE/AT inhibitor or inotropic agents, cardiopulmonary resuscitation (CPR) 24h before surgery, emergency surgery, type of surgery (CABG, CABG + valve surgery, CABG + other, valve surgery or other) and EuroSCORE I.

Propensity score BT-2

Zijn er niet-JG getransfundeerd met 1 RBC met een laagste **Hb <8 g/dL** ($\approx 4,9$ mmol/L) of een peroperatieve **Hb-daling van $\geq 50\%$** ?

Voor 831 van deze 1015 patienten kon een niet-getransfundeerde niet-JG patient gevonden worden met een vergelijkbare BT-propensity score (nearest neighbour)

Non-transfused vs 1 RBC

Table 3: Patient Characteristics in patients with an intra-operative Hb < 8 g/dL and/or a intra-operative Hb decrease of \geq 50%

| | Total (N=1662) | Non-Transfused patients (N=831) | Transfused Patients (1 units) (N=831) |
|--------------------------------------------|-----------------------|---------------------------------------|------------------------------------------------|
| Pre-operative variables | | | |
| Propensity score, median (IQR) | 0.2653(0.1630-0.3966) | 0.2654(0.1629-0.3967) | 0.2653(0.1630-3966) |
| Age, median (IQR) | 72(65-77) | 72(65-77) | 72(65-77) |
| Female, N (%) | 1075(64.7) | 537(64.6) | 538(64.7) |
| Weight (kg), median (IQR) | 71(63-80) | 71(64-80) | 70(63-80) |
| Year of surgery, median (IQR) | 2005(2002-2008) | 2005(2002-2008) | 2005(2001-2009) |
| Previous cardiac surgery, N (%) | 127(7.6) | 65(7.8) | 62(7.5) |
| Smoking, N (%) | 236(14.2) | 123(14.8) | 113(13.6) |
| Pre-operative Hb level, g/dl, median (IQR) | 12.6(11.8-13.4) | 12.6(11.8-13.4) | 12.6(11.8-13.4) |
| Hypercholesterolemia, N (%) | 1049(63.1) | 521(62.7) | 528(63.5) |

Non-transfused vs 1 RBC

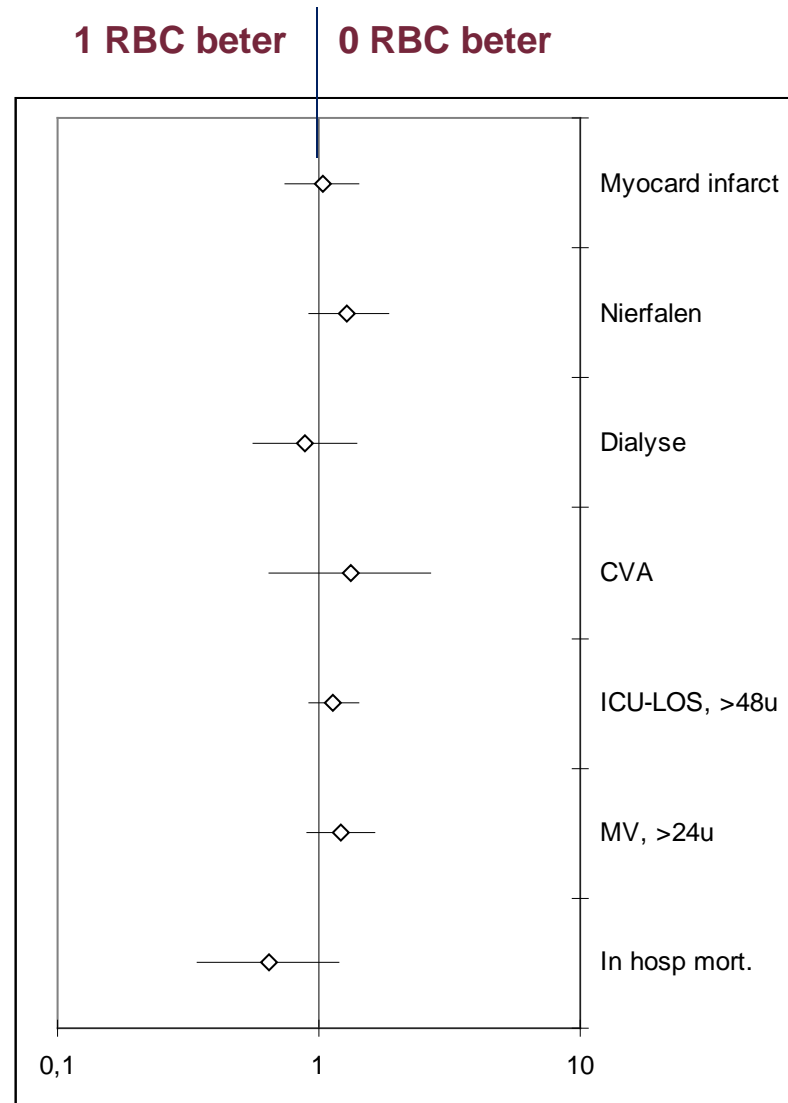
Table 4: Postoperative Outcomes in patients with an intra-operative nadir Hb < 8 g/dL and or an intra-operative Hb decrease \geq 50%

| | Non-Transfused patients (N =831) | Transfused patients (1 units) (N =831) | Crude OR (95% CI) | aOR* (95% CI) |
|-----------------------------------------------------|-------------------------------------|----------------------------------------------|----------------------|------------------|
| - Myocardial infarction, N (%) | 83(10.0) | 88(10.6) | 1.07(0.78-1.47) | 1.03(0.74-1.42) |
| - Acute kidney injury, N (%) | 64(7.7) | 84(10.1) | 1.35(0.96-1.89) | 1.29(0.91-1.84) |
| - CVVH de novo, N (%) | 42(5.1) | 43(5.2) | 1.03(0.66-1.59) | 0.89(0.56-1.40) |
| - Stroke, N (%) | 15(1.9) | 18(2.4) | 1.20(0.60-2.41) | 1.33(0.65-2.68) |
| - ICU length of stay (hours), median (IQR) | 24(20-48) | 24(21-63) | | |
| - ICU length of stay > 48 hours, N (%) | 206(24.8) | 233(28.0) | 1.18(0.95-1.47) | 1.14(0.91-1.43) |
| - Mechanical ventilation time (hours), median (IQR) | 10(7-14) | 10(7-16) | | |
| - Mechanical ventilation > 24 hours, N (%) | 96(11.6) | 112(13.5) | 1.19(0.89-1.60) | 1.21(0.90-1.64) |
| - In hospital mortality, N (%) | 30(3.6) | 20(2.4) | 0.66(0.37-1.17) | 0.64(0.34-1.19) |
| - Hb level at discharge (g/dL), median (IQR) | 10.0(9.3-10.8) | 10.1(9.5-10.9) | | |
| - Composite endpoint**, N (%) | 149(17.9) | 144(17.3) | 1.04(0.81-1.34) | 0.94(0.72-1.23) |

* Adjusted for: time in surgery, CPB duration, intra-operative circulatory arrest, cell saver blood returned during surgery, intra-operative nadir Hb (g/dL)

** Composite endpoint consisting of: Myocardial infarction, CVVH, Stroke, in hospital mortality

1 RBC versus geen RBC



Samenvatting

Zowel bij JG als bij niet-JG, is anemie (Hb<8 g/dL) geassocieerd met een slechtere prognose.

Bij een nadir Hb <8 g/dL resulteert het ontvangen van 1 RBC niet in een slechtere prognose.

(tov JG en tov niet-getransfundeerde niet-JG)

Zwakke / sterke punten

- Resterende confounding (niet weten/gemeten)
 - “Nettere”/drogere chirurgie bij JG
 - Alleen naar 1 RBC gekeken, niet naar >1 RBC
- + Effect van anemie bij JG en niet-JG
- + Naast JG vs 1 RBC, ook niet-JG: 0 RBC vs 1 RBC

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Vragen?

