

Science Letter

Peri-operative haemoglobin trajectories in patients without pre-operative anaemia undergoing valvular heart surgery

Anaemia is common in patients undergoing cardiac surgery and is associated with adverse clinical outcomes [1, 2]. While pre-operative anaemia is a well-established prognostic factor [1, 2], the clinical significance of postoperative anaemia and haemoglobin recovery are less well understood [3]. In our previous study [4], we showed that persistent postoperative anaemia, defined as haemoglobin $< 100 \text{ g.l}^{-1}$ at 2 months, was associated independently with 1-year mortality, with particularly high risk in patients who developed postoperative anaemia despite normal pre-operative levels. To further explore the temporal dynamics of haemoglobin recovery, we analysed extended peri-operative haemoglobin trajectories in patients without pre-operative anaemia undergoing open valvular heart surgery.

Of 2486 patients who underwent surgery from 1 January 2016 to 31 July 2023, 1379 had no pre-operative anaemia, according to the World Health Organization (WHO) criteria [5]. Longitudinal haemoglobin profiles were constructed using daily measurements during hospitalisation and follow-up at 2 weeks and 2 months, 6 months and 12 months. Patients were stratified by postoperative anaemia status, and peri-operative haemoglobin trends were compared using the Mann–Whitney U-test. Individual time-point comparisons were interpreted with a Bonferroni correction applied. The interaction term from a linear mixed model was used to assess whether haemoglobin change differed between the groups over time. Patient characteristics and clinical outcomes, including previously identified risk factors for postoperative anaemia [4], were compared between the groups using the Mann–Whitney U-test for continuous variables and the χ^2 or Fisher's exact tests for categorical variables.

Among 1379 patients without pre-operative anaemia, 61 (4%) developed postoperative anaemia. The overall median (IQR [range]) pre-operative haemoglobin was 137 (130–145 [120–197]) g.l $^{-1}$. The nadir occurred on postoperative day 4 at 88 (81–96 [50–154]) g.l $^{-1}$, followed by gradual recovery to 127 (117–136 [51–170]) g.l $^{-1}$ at 2 months and 137 (127–148 [72–179]) g.l $^{-1}$ at 1 year. Patients who developed postoperative anaemia had

significantly lower baseline haemoglobin (133 vs. 137 g.l $^{-1}$, $p = 0.002$) and lower immediate (postoperative day 0–2) haemoglobin levels (all $p < 0.004$). Haemoglobin levels converged at postoperative days 3–5 with no significant differences, while from postoperative day 6 onwards, patients with postoperative anaemia consistently showed lower haemoglobin levels, with differences widening throughout the 1-year follow-up period (all $p < 0.004$). The interaction between time and anaemia was significant ($p < 0.001$), confirming divergent recovery trajectories (Fig. 1).

Patients with postoperative anaemia showed higher pre-operative red blood cell distribution width; longer cardiopulmonary bypass time; greater intra-operative transfusion; and more postoperative complications (Table 1). The proportion of women with borderline anaemia (120–129 g.l $^{-1}$), classified as non-anaemic by the WHO criteria, was significantly greater in the anaemia group (41% vs. 24%, $p = 0.004$).

Our extended analysis highlights that haemoglobin recovery after valvular heart surgery follows distinct trajectories according to new development of persistent postoperative anaemia, and that these haemoglobin differences remain separated for up to 1 year. Even before surgery, patients who later developed postoperative anaemia had significantly lower, though still normal, pre-operative haemoglobin levels according to the WHO criteria. This subtle difference suggests the presence of an underlying predisposition or reduced haematological reserve, which may not be captured by standard anaemia definitions. Specifically, women in the postoperative anaemia group were disproportionately represented among those with borderline pre-operative anaemia, highlighting the limitations of sex-specific cut-offs and suggesting reduced haematological reserve in this subgroup [6].

Our findings suggest that postoperative anaemia is not simply a transient effect of surgical blood loss or haemodilution but reflects impaired erythropoietic recovery or ongoing physiological stress [7]. The divergence in haemoglobin recovery, apparent from postoperative day 6, marks an early convalescent phase

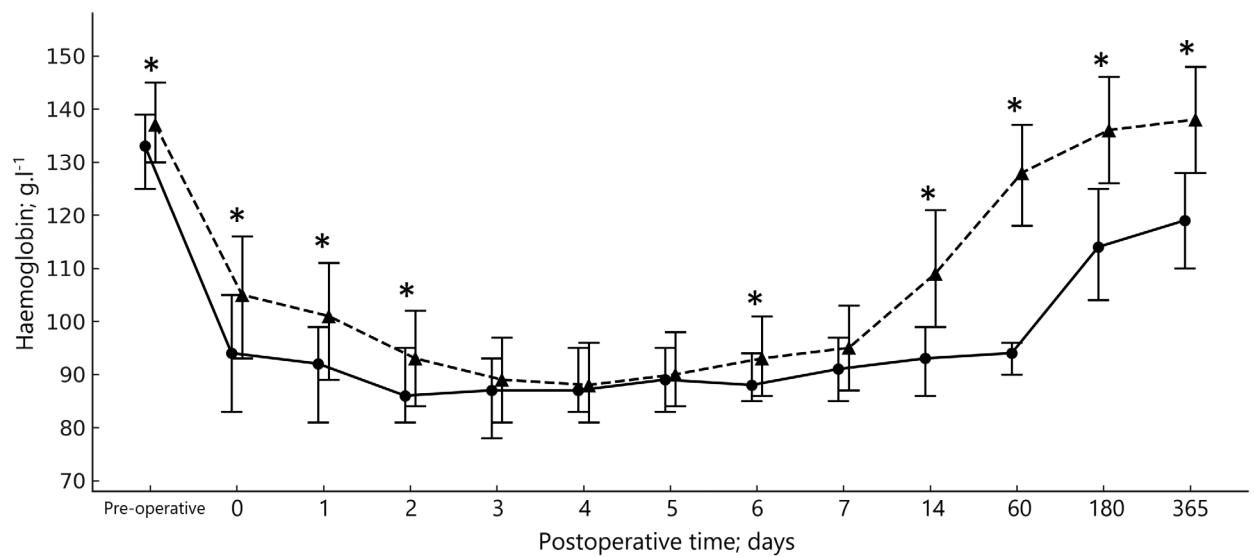


Figure 1 Peri-operative haemoglobin concentration trends according to postoperative anaemia status. Values are presented as median with error bars showing the IQR. Circle with solid line, postoperative anaemia; triangle with dashed line, no postoperative anaemia. Interaction p value between time and postoperative anaemia status <0.001 . Missing data: postoperative day 3 = 35 (3%); postoperative day 4 = 150 (11%); postoperative day 5 = 279 (20%); postoperative day 6 = 306 (22%); postoperative day 7 = 465 (34%); postoperative day 14 = 5 (<1%); postoperative day 180 = 212 (15%); postoperative day 365 = 590 (43%). * $p < 0.0038$ by Mann–Whitney U-test using Bonferroni adjustment.

Table 1 Patient characteristics and risk factors for the development of postoperative anaemia according to postoperative anaemia status in patients without pre-operative anaemia. Values are median (IQR [range]) or number (proportion).

Time	Total n = 1379	Patients with postoperative anaemia n = 61	Patients without postoperative anaemia n = 1318	p value
Age; y	64 (55–70 [18–90])	67 (60–74 [32–90])	63 (54–70 [18–87])	0.002
Sex; female	676 (49%)	40 (66%)	636 (48%)	0.012
EuroSCORE-2	2 [1–4 [0–21]]	3 (2–7 [1–16])	2 (1–4 [0–21])	< 0.001
1-year mortality	14 (1%)	8 (13%)	6 (< 1%)	< 0.001
Pre-operative red cell distribution width; %	13 (13–14 [11–24])	13 (13–14 [12–24])	13 (13–4 [11–20])	< 0.001
Cardiopulmonary bypass time; min	92 (69–120 [26–541])	120 (95–149 [49–541])	90 (68–120 [26–430])	< 0.001
Intra-operative allogeneic red blood cell transfusion	289 (21%)	31 (51%)	258 (20%)	< 0.001
Sustained postoperative complication	440 (32%)	38 (62%)	402 (31%)	< 0.001

when persistent anaemia becomes clinically distinguishable. Postoperative anaemia could be a potential marker and mediator of extended vulnerability after valvular heart surgery. Whether active intervention to correct postoperative anaemia can improve clinical outcomes remains uncertain and warrants further investigation.

Patients without pre-operative anaemia who developed anaemia postoperatively, defined as haemoglobin < 100 g.l $^{-1}$ at 2 months, showed persistently impaired haemoglobin recovery, with progressively widening differences evident from discharge up to 1 year. This trajectory was significantly associated with increased

1-year mortality, highlighting postoperative anaemia as an early marker of prolonged risk.

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