Universal Library of Medical and Health Sciences
Short Communication

ISSN: 3064-6545 | Volume 2, Issue 2

Open Access | PP: 24-27

DOI: https://doi.org/10.70315/uloap.ulmhs.2024.0202005

Does Preoperative Anemia Influences Postoperative Mortality After Isolated CABG? A Sequential Analysis

Thierry CAUS[1], Toufik IAICHE[2]

[1]University Hospital Amiens-Picardie, Amiens, France.

[2]University Hospital Nafissa-Hamoud, Alger, Algérie.

Abstract

The potential impact of preoperative anemia on postoperative mortality after CABG is becoming widely endorsed by best practice guidelines in patient blood management. However clinical evidences are still scarce and very large number of patients are needed to prove certainty in preemptive therapeutic measures like iron substitution. We aimed at illustrate the usefulness of CUSUM in this setting and reviewed a historical series of 1282 patients operated on for isolated CABG. The negative effect of preoperative anemia on fatal outcome after CABG could be assessed with an unacceptable rate of failure after 266 anemic patients only. This should encourage trials based on sequential analysis with the hope to fasten emergence of conclusive results.

Keywords: *Coronary surgery, Control Charts, Cusum, Anemia, Outcomes.*

INTRODUCTION

Retrospective studies and very large registries have shown worsen outcomes after CABG for patients requiring transfusions of even small quantities of postoperative blood products [1,2]. Besides, patients without preoperative anemia, are less likely to require heterologous blood transfusion during in hospital course and it is now recommended as a good clinical practice to treat all surgical patients with pre-operative iron deficiency anemia, in particular those for which a major surgery is considered [3]. An extrapolation of this recommendation has been addressed to coronary artery bypass grafting with or without extra-corporeal circulation [4]. However evidences are still scarce to establish a direct correlation between preoperative anemia, a common feature [5] and worsen outcomes after CABG [6,7]. Though, intuitively considering preoperative anemia as a modifiable risk factor of postoperative mortality might be an interesting issue, it is still an hypothesis under investigation with conflicting results. Implementing PBM on a large scale has proven to be effective in reducing blood products consumption but not in decreasing global mortality and morbidity in general surgery [8]. However the efficacy of intravenous iron for treatment of anemia before cardiac surgery has been shown to be associated with a decrease in mortality but not with a reduction of the rate of transfusion requirement in a recent meta-analysis [9].

In this context, we aimed at establishing a new tool to study clinical outcomes in anemic patients undergoing isolated coronary surgery, and possibly to assess the efficacy of institutional PBM programs in this setting. This tool is based on sequential analysis, which is known to require less patient inclusions to obtain conclusive results [10]. We present here an illustration of its use through studying the impact of preoperative anemia on in hospital mortality after isolated CABG in an historical cohort.

PATIENTS AND METHODS

We conducted this observational retrospective and monocentric study including all patients operated on in our center for isolated CABG between January 2008 and June 2017. This included patients operated on in emergency or upon mechanical support following cardiac rescue at the exclusion of patients who presented mechanical complications of myocardial infarction. Among many other datas, we considered as variables of interest the value of preoperative hemoglobin level and in hospital mortality defined as any death undergoing before patient's discharge. Patients were therefore categorized into two groups according to the WHO definition for anemia depending on sex gender (ie under 13g/dL and 12g/dL for men and women respectively) . To analyze the effect of preoperative anemia on in-hospital mortality, we constructed cumulative sum (CUSUM) graphs of failure assuming a postoperative mortality between 2.5 and 4% which represented the range of the null hypothesis. This percentage of lower and higher alarm setup for postoperative mortality were extracted from the funnel plot representing results of CABG surgery on a national level during study time (not published). Due to the observational nature of the study and in compliance to best practices in clinical studies, the national ethic committee waived the need of inform patient's consent.

STATISTICS

CUSUM graphs were constructed very affordably with Microsoft® Excel [11]. Following the rule of sequential analysis, graph construction was performed patient per patient, without any adjustment to preoperative risk, upon the formula: Jn=In+Jn-1 where In represents the outcome value for the patient n and Jn-1 represents the value of the CUSUM for the patient n-1. Therefore the total number of patients is reported on the horizontal axis and the cumulative observed in-hospital mortality is reported on the vertical axis. After setting p0 and p1 value at the border of the desired mortality rate (ie p0= 0.025 and p1=0.04), lines for alarm signals (cumulative failure rates at unacceptable level) were constructed upon the formula: Sn +/- a (P+Q) where S=Q/ P+Q, P=Ln (p1/p0) and Q=Ln (1-p0)/(1-P1). Lines for alert zones (cumulative failure rates at a still acceptable level) were constructed upon the formula Sn +/- b (P+Q). Values of a and b were calculated after setting type 1 and type 2 error rates at 0.05 and 0.2 respectively upon the formulae: a = Ln [(1-type 2 error rate)/type 1 error rate] and b= Ln [(1-type 1 error rate)/type 2 error rate].

RESULTS

A total of 1282 patients (normalized sex ratio 391:100) were included among which 403 (31.4%) were anemic and 45 (3.5%) died postoperatively. Table 1 resumes principal data from clinical presentation and procedural features. Anemic patients were more likely to be older (p<0.0001) and women proportion was also greater in that group (p<0.0001). As regards to preoperative risk as assessed by the Euroscore risk scale, anemic patients presented a significantly higher Log Euroscore (p<0.0001), however the absolute difference was only 0.3. Patients from both groups anemic and non anemic underwent OPCAB surgery and complete arterial grafting in comparable proportions. Patients receiving more than four distal anastomoses were also comparably represented in both groups. Figure 1 depicts distribution of men/women according to the preoperative hemoglobin level. Figure 2 illustrates the incidence of preoperative hemoglobin concentration on in-hospital mortality from all causes following CABG.

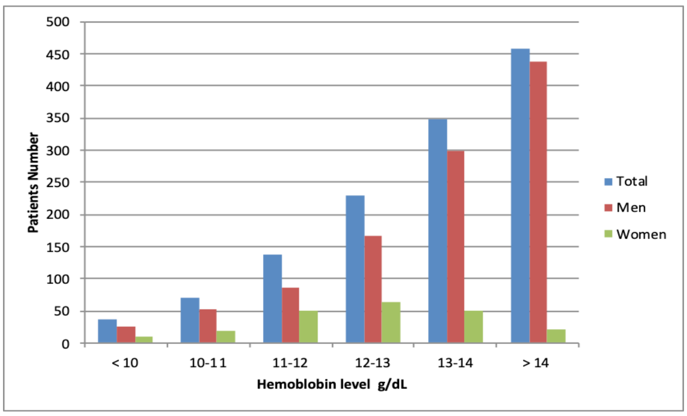

Figure 1. Proportion of men versus women for different levels of preoperative hemoglobin concentration.

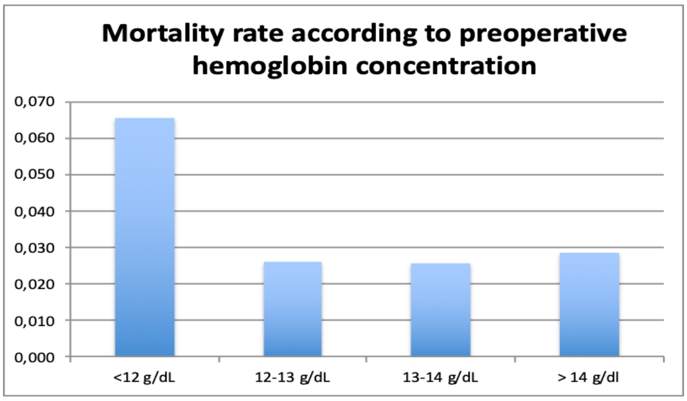

Figure 2. Influence of preoperative concentration of hemoglobin on in-hospital mortality.

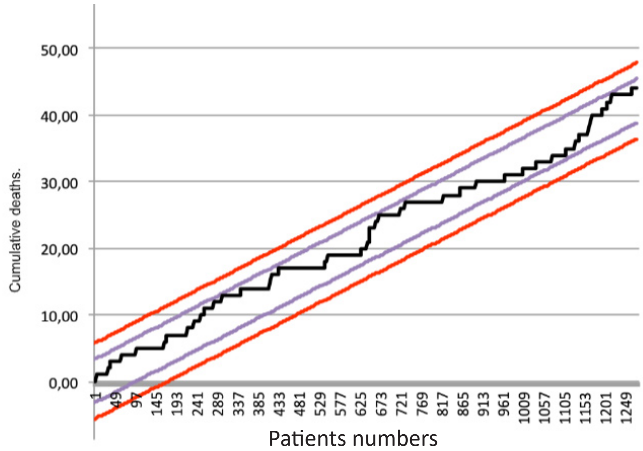

Figure 3. Cumulative sum chart of in-hospital death (Overall population). Purple lines represent lower and upper limit for an alert signal. Red lines represent lower and upper limits for an alarm signal.

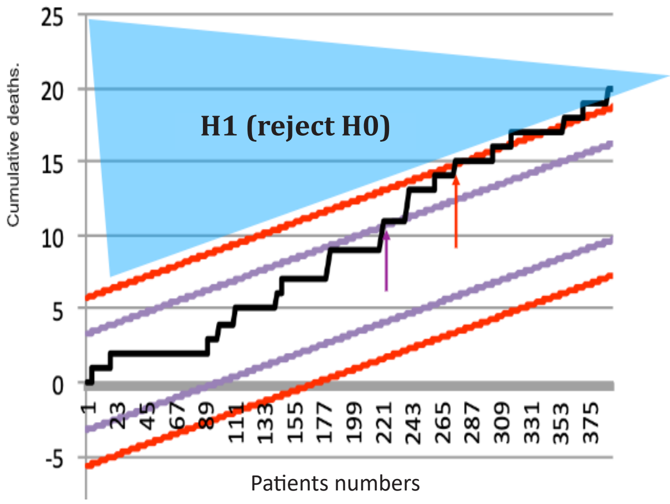

Figure 4. Cumulative sum chart of in-hospital death for anemic patients. Purple lines represent lower and upper limit for an alert signal. Red lines represent lower and upper limits for an alarm signal.

Figure 3 represents the CUSUM chart of in-hospital death for the overall population. The chart remains constantly in the safety zone between upper and lower alert lines meaning that though the null hypothesis is not demonstrated for the overall population, the observed mortality during study time remains kept between the pre-determined borders of 2.5% and 4%. Figures 4 and 5 represent CUSUM charts of in-hospital death for the anemic and non-anemic patients respectively. For anemic patients, the CUSUM crosses the upper alert and alarm lines for patient 243 and 266 respectively. Therefore H1 is accepted meaning a postoperative mortality significantly above 4% (p<0.01) in case of preoperative anemia. For non-anemic patients, the CUSUM crosses the lower alert and alarm lines for patients 501 and 619 respectively. Therefore H0 is definitely accepted for non-anemic patients.

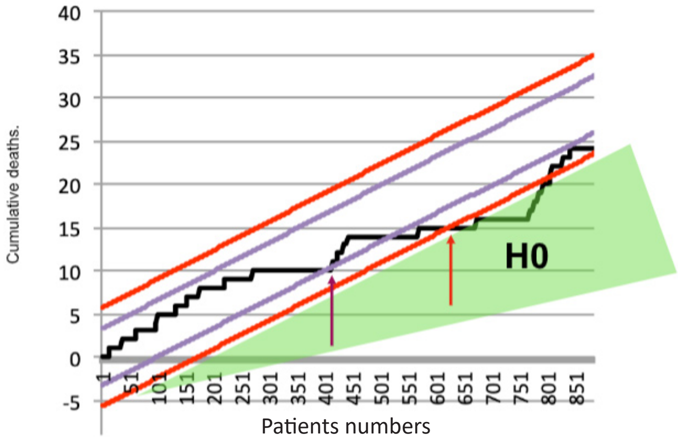

Figure 5. Cumulative sum chart of in-hospital death for non-anemic patients. Purple lines represent lower and upper limit for an alert signal. Red lines represent lower and upper limits for an alarm signal.

DISCUSSION

In the setting of coronary surgery preoperative anemia worsens myocardial ischemia and increases the likelihood for hemodynamic instability which can precipitate the decision for surgery. Preoperative anemia also is a strong predictor of perioperative allogeneic blood transfusion with a dose-dependent relationship between the amount of transfused products with a composite outcome of myocardial infarction, stoke, pulmonary, renal, septic and wound complications [12].

We confirmed in our study the considerable prevalence of preoperative anemia in patients undergoing CABG surgery [5]. By sequential analysis in-hospital mortality after isolated CABG is significantly increased (p<0.01) in case of preoperative anemia. Noticeably, despite a twofold increase in post operative mortality in case of preoperative anemia, classical statistics based on variance analysis did not allow to conclude for a significant difference in our study (Table 1). Had we wanted to prove by conventional statistics that observed difference was significant, we would have to include 1313 patients in each group (for a α value at 0.05 and a β value at 0.2). Hence a significant difference in postoperative outcome could be established with fewer patients by use of CUSUM which, usually used for quality management, could also become a new standard to observe impact of one variable on any binary outcome in clinical studies. If the main finding of the study is not new [6,7], considering the already existing literature and the fact that recognize and treat preoperative anemia clearly supports one of the three pillars of patient blood management (PBM) [13], we believe that the original method we used to establish this finding could be appropriately used to assess the effects of any institutional PBM policy on outcomes without awaiting to be able to study very large cohorts.

Table 1. Main patients characteristics in both groups.

	Anemic (n= 403)	Non anemic (n=879)	p
Age	68.2 +/- 10	65.5 +/- 10	<0.0001
Men (%)	299 (74.2)	766 (83.7)	<0.0001
Log Euroscore	4.7 +/- 0.5	4.4 +/- 0.6	<0.0001
OPCAB (%)	41 (10.2)	110 (12.5)	0.25
Distal anastomoses > 3 (%)	23 (5.7)	64 (7.2)	0.31
All arterial grafting (%)	141 (35)	351 (40)	0.08
Overall in-hospital mortality (%)	20 (4.9)	25 (2.8)	0.056

OPCAB: Off pump coronary artery bypass.

One main interest of CUSUM charts is indeed that they allow to assess results step by step (ie. after each patient inclusion) without awaiting that the specific pre-calculated number of patients to be included is obtained. In other words « sequential analysis is a statistical method in which the final number of patients analyzed is not predetermined, but sampling or enrollment of patients is decided by a predetermined stopping rule such as satisfying a statistical significance. Accordingly, the investigators may draw a conclusion earlier than that with the traditional statistical methods, reducing time, cost, effort, and resources.. » and sequential analysis could also be used to perform meta-analysis of effects of anemia or PBM on operative outcome after CABG through a review of existing literature [14].

One important limitation is that CUSUM charts do not allow to determine if the studied variable has an independent effect on the observed outcome. In our study, it has to be acknowledge that anemic patients were significantly older and presented with a higher Log-Euroscore, both factors tending to increase postoperative mortality after CABG. Unfortunately, because we focussed on an historical series, numerous other variables which could have alter early survival might have been definitely missed and observed mortality in the present series do not reflect contemporary results after CABG which endorse a much lower postoperative mortality (near or below 1%). However, the series we present here can serve as a base to a « before-after » type study which we are aiming to conduct to assess the benefits of PBM in CABG surgery.

CONCLUSION

Preoperative anaemia is a common feature in coronary surgery and indeed increases operative mortality after isolated CABG. The number of patients needed to be included in the study is lower when results are monitored with sequential analysis which therefore sharpens identification of risk-factors for in-hospital mortality. Our results confirm the importance of preoperative anaemia as a potentially modifiable risk factor in isolated coronary surgery.

REFERENCES

1. Girardi NI, Cushing MM, Evered LA, et al. Incidence and Impact of a Single-Unit Red Blood Cell Transfusion: Analysis of The Society of Thoracic Surgeons Database 2010-2019. Ann Thorac Surg2023; 115(4):1035-1041.
2. Paone G, Likosky DS, Brewer R, et al. Transfusion of 1 and 2 units of red blood cells is associated with increased morbidity and mortality. Ann Thorac Surg. 2014;97:87-94.
3. Muñoz M, Acheson AG, Auerbach M, et al. International consensus statement on the peri-operative management of anaemia and iron deficiency. Anaesthesia 2017;72:233–247
4. Mertes PM, Kindo M, Amour J, et al. Guidelines on enhanced recovery after cardiac surgery under cardiopulmonary bypass or off-pump. Anaesth Crit Care Pain Med. 2022 Jun;41(3):101059.
5. Klein AA, Collier TJ, Brar MS. The incidence and importance of anaemia in patients undergoing cardiac surgery in the UK - the first Association of Cardiothoracic Anaesthetists national audit. Anesthesia. 2016 Jun;71(6):627-35.
6. Miceli A, Romeo F, Glauber M, et al. Preoperative mortality increases mortality and postoperative morbidity after cardiac surgery. J Cardiothorac Sur. 2014;9:137.
7. Scrascia G, Guida P, Caparrotti SM, et al. Incremental value of anemia in cardiac surgery risk prediction with the EUROSCORE II model. Ann Thorac Sur 2014;98:869-75.
8. Meybohm P, Schmitt E, Choorapoikayil S et al. German Patient Blood Management Network: effectiveness and safety analysis in 1.2 million patients. British Journal of Anaesthesia 2023; 131 (3): 472e481.
9. Liu HM, Tang XS, Yu H ans Yu H. The efficacy of intravenous ironfor treatment of anemia before cardiac surgery: An updated systematic reviewand meta-analysis with trial sequential analysis. J CardioThorac Surg 2023; 18: 16.
10. Davies OL. The design and analysis of industrial experiments. Published for Imperial Chemical Industries Limited. Oliver and Boyd. London. 1956.
11. Noyez L. Control charts, Cusum techniques and funnel plots. A review of methods for monitoring performance in healthcare.
12. Bernard AC, Davenport DL, Chang PK, Vaughan TB, Zwischenberger JB. Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mor- tality, surgical-site infection, pneumonia, and sepsis in general surgery patients. *J Am Coll Surg*. 2009;208:931–937, 937.e1.
13. Desal N, Schofield N, Richards T. Perioperative patient blood management to improve outcome. Anesth Analg 2018;127:1211-20.
14. Trial sequential analysis: novel approach for meta-analysis. Kang H. Anesth Pain Med 2021;16(2):138-150.

Citation: Thierry CAUS, Toufik IAICHE, “Does Preoperative Anemia Influences Postoperative Mortality After Isolated CABG? A Sequential Analysis”, Universal Library of Medical and Health Sciences, 2024; 2(2): 24-27. DOI: https://doi.org/10.70315/uloap.ulmhs.2024.0202005.