Correspondence

Letter Regarding Article by McKechnie et al, “Prognostic Implication of Anemia on In-Hospital Outcomes After Percutaneous Coronary Intervention”

To the Editor:

With great interest we have read the article by McKechnie and colleagues1 about the higher rates of in-hospital mortality in anemic patients undergoing percutaneous coronary intervention (PCI). In brief, they observed in their analysis of 45 165 patients in the quartile with the lowest hemoglobin concentrations (men: 6.6 to 10.1 g/dL; women: 5.4 to 9.5 g/dL) an in-hospital mortality rate for men of 5.0% compared with 2.8%, 1.9%, and 1.9% in the other quartiles, respectively (women: 3.2% versus 2.6%, 2.2%, and 1.8%, respectively). Of note, a relevant number of PCI patients had acute (16.3%) or recent myocardial infarctions (33.5%), and 2.3% had cardiogenic shock.

These results are complementary to previous findings of our group, in which we assessed the short- and long-term outcomes of 689 men who underwent elective PCI.2 In contrast, we found similar in-hospital outcomes in the lowest hemoglobin quintile (8.5 to 12.9 g/dL) as compared with the other quintiles. This might be the result of higher hemoglobin concentrations in our lowest quintile and the high proportion of patients with myocardial infarction study in the study of McKechnie and associates. We, however, focused on elective PCIs. During follow-up (median 697 days), using Kaplan-Meier models, we found a significantly higher mortality rate in patients of the lowest hemoglobin quintile (22.2%) as compared with the others (7.3%). Analyses of the causes of death revealed that the higher mortality rate in the lowest hemoglobin quintile was the result of cardiovascular death and not cancer or other causes. Moreover, a U-shaped mortality curve was observed when plotted against hemoglobin concentrations, with significantly higher mortality rates <11.0 g/dL and >18.0 g/dL.

In our opinion, these 2 studies, together with the epidemiological data gathered by Sarnak et al.,3 provide consistent evidence about the amazing impact of anemia (apart from its etiology) on cardiovascular mortality. Pathophysiologically, anemia is accompanied by tissue hypoxia and leads to activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system, thereby inducing tachycardia and retention of salt and water. In combination with long-term consequences such as left ventricular hypertrophy and dilatation, which further increase oxygen consumption, these may be deleterious factors in anemic patients with coronary stenoses and myocardial ischemias.4 Because anemia is so often undiagnosed and untreated5 and is a common condition in the general population, and coronary artery disease and related coronary interventions also are common, further trials should evaluate strategies to lower the high mortality rates in this large subset.

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Response

We read with interest the letter by Drs Reinecke and Breithardt about our recent article on the prognostic implication of anemia in in-hospital outcomes after percutaneous coronary intervention (PCI). In our study,1 we found that regardless of the definition of anemia used, anemia was independently associated with an increased risk of in-hospital death in men and of major adverse events in men and women. Whereas our analysis was focused on a large group of patients (29 844 men and 15 321 women) undergoing contemporary PCI for stable and unstable coronary syndromes, the study of Reinecke et al was focused on a small group of men (689 patients) undergoing elective PCI.2 Differences in sample size and substantial differences in the patient populations can explain the difference between the 2 studies with regard to the effect of anemia on acute in-hospital outcomes. In our study, the unadjusted mortality rate was 0.58% in 1905 anemic men undergoing elective PCI and 0.15% in 8633 nonanemic men undergoing elective PCI (P<0.001). In contrast, the mortality rates were, respectively, 11.8% and 3.15% in anemic and nonanemic men undergoing PCI for acute myocardial infarction (P<0.0001). The issue of sample size cannot be overemphasized, given the relatively low risk of adverse outcomes in patients undergoing elective PCI, and given that in Dr Reinecke’s study there were only 3 in-hospital deaths in the 689 patients studied. We agree with Dr Reinecke that the 2 studies complement each other because they focus attention on the poor prognostic implication of anemia for both short- and long-term outcomes after PCI. Although we agree that the presence of anemia is accompanied by tissue hypoxia leading to the activation of neurohormonal pathways, which may result in a chain of adverse events, we also believe that it cannot be excluded that anemia in this patient population might be an overall marker of disease severity, and that as such it is associated with an increased risk of adverse outcomes. Finally, whether optimization of hemoglobin levels before PCI may be of clinical benefit remains to be determined, particularly in view of the current controversy about the use of blood transfusion in patients with acute coronary syndromes.3,4 Besides transfusion, future options could include the periprocedural use of erythropoietin or the urgent use of synthetic blood substitutes. A series of randomized studies will be needed to determine the value of these therapeutic interventions in this patient population.

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1. McKechnie RS, Smith D, Montoye C, Kline-Rogers E, O’Donnell MJ, DeFranco AC, Meens WL, McNamara R, McGinnity JG, Patel K, Share D, Riba A, Khanal S, Moscucci M; Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2). Prognostic implication of anemia on in-hospital outcomes after percutaneous coronary intervention (PCI). In our study, we found that regardless of the definition of anemia used, anemia was independently associated with an increased risk of in-hospital death in men and of major adverse events in men and women. Whereas our analysis was focused on a large group of patients (29 844 men and 15 321 women) undergoing contemporary PCI for stable and unstable coronary syndromes, the study of Reinecke et al was focused on a small group of men (689 patients) undergoing elective PCI. Differences in sample size and substantial differences in the patient populations can explain the difference between the 2 studies with regard to the effect of anemia on acute in-hospital outcomes. In our study, the unadjusted mortality rate was 0.58% in 1905 anemic men undergoing elective PCI and 0.15% in 8633 nonanemic men undergoing elective PCI (P<0.001). In contrast, the mortality rates were, respectively, 11.8% and 3.15% in anemic and nonanemic men undergoing PCI for acute myocardial infarction (P<0.0001). The issue of sample size cannot be overemphasized, given the relatively low risk of adverse outcomes in patients undergoing elective PCI, and given that in Dr Reinecke’s study there were only 3 in-hospital deaths in the 689 patients studied. We agree with Dr Reinecke that the 2 studies complement each other because they focus attention on the poor prognostic implication of anemia for both short- and long-term outcomes after PCI. Although we agree that the presence of anemia is accompanied by tissue hypoxia leading to the activation of neurohormonal pathways, which may result in a chain of adverse events, we also believe that it cannot be excluded that anemia in this patient population might be an overall marker of disease severity, and that as such it is associated with an increased risk of adverse outcomes. Finally, whether optimization of hemoglobin levels before PCI may be of clinical benefit remains to be determined, particularly in view of the current controversy about the use of blood transfusion in patients with acute coronary syndromes.3,4 Besides transfusion, future options could include the periprocedural use of erythropoietin or the urgent use of synthetic blood substitutes. A series of randomized studies will be needed to determine the value of these therapeutic interventions in this patient population.

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