Letter to Editor:

Comment on "Preoperative Intravenous Iron Therapy and Survival after Colorectal Cancer Surgery: Long Term Results from the IVICA Randomised Controlled Trial"

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Dear Editor,

We read with interest the article by Dickson et al. reporting long term follow up of the IVICA trial, comparing parenteral iron to oral iron to correct preoperative anaemia in patients undergoing surgery for colorectal cancer (CRC) [1]. The original randomised controlled trial in 116 patients found no significant difference in postoperative blood transfusion requirement between the two methods of iron replacement in anaemic patients undergoing surgery for stage I-III disease [2]. In this long term follow up study, the authors report no significant difference in overall (OS), cancer specific (CSS) or disease free survival (DFS) between the treatment groups. The results do however suggest that correction of anaemia prior to surgery may be associated with improved OS at up to 5 years following surgery for CRC [1].

The recently published PREVENTT trial, comparing preoperative intravenous iron to placebo in patients with anaemia undergoing major abdominal surgery, like the IVICA trial, found no difference in blood transfusion requirement in the treatment group [3]. It is our concern, therefore, that the legacy of these trials will be the widespread and immediate abandonment of preoperative assessment of iron status, and correction of iron deficiency in those with anaemia. This is despite the long term benefits suggested by IVICA, and PREVENTT itself demonstrating sustained correction of anaemia, reduced re-admission rate due to complications, with a reduction in pain, ileus, wound infection and other infection after discharge, in those in the treatment group.

In our experience of patients with colorectal cancer undergoing elective resection, multiple mechanisms underly the aetiology of preoperative anaemia [4], with a high prevalence of functional iron deficiency (FID) and anaemia of inflammation (AOI). Furthermore, these

mechanisms demonstrate a differential response to treatment with parenteral iron [5]. It is therefore important that future studies of preoperative iron replacement include patients who meet the definition of IDA undergoing specified types of open and minimally invasive surgery, that current blood transfusion requirement estimates are used to derive sample sizes, and that a combination of perioperative blood transfusion and objective measures of postoperative recovery and survival are used as co-primary outcomes. Additional research on the effectiveness of parenteral iron is required in the significant proportion of patients with FID or AOI, and they should not be inappropriately grouped alongside IDA.

Whilst the results of the PREVENTT trial may be considered by some to signal the end of preoperative iron replacement, they should perhaps be seen as the return of equipoise needed to conduct further trials in this important area. Indeed, this long term follow up study from the IVICA trial hints at the possible significant long term gains which may be made by identifying and correcting preoperative anaemia, and should encourage further research in this area.

References:

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