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Letter to the editor

See also a meta-analysis on vitamin C and AF published after the submission of this letter:

Hemilä H, Suonsyrjä T.
Vitamin C for preventing atrial fibrillation in high risk patients: a systematic review and meta-analysis [meta-analysis]. BMC Cardiovascular Disorders 2017;17:49
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Antonic et al. reported the findings of a randomized trial on vitamin C and atrial fibrillation (AF) [1]. They wrote that “the sample size estimation was based on the assumption that the incidence of AF after CABG lies at about 25% and that the administration of ascorbic acid would result in a 20% decrease of AF. With a power of 80%, beta error of 0.2 and alpha of 0.05, about 50 patients were required in each group” [1]. This sample size calculation does not seem to be correct. The calculation can be easily checked, since there are sample size calculators available on the web [2,3].

Antonic et al. assumed that the proportion of patients who suffer from AF is 25% in the non-treated group and that vitamin C would decrease that rate by 20%, which leads to AF incidence of 20% (=0.80*25%) in the vitamin C group. With these assumed proportions, 25% and 20%, and also the assumed beta and alpha levels, the sample size calculators give 1092 to 1134 patients per group as adequate sample sizes, depending on the details of the calculation [2,3]. Thus, the published calculation that 50 patients in each group is sufficient seems to be incorrect.

Antonic et al. apparently assumed in their calculation that the effect of vitamin C was an 80% decrease in the AF rate, which is complementary to the published assumption of 20% effect (100% - 20% = 80%). Assuming that the AF rate is 25% in the non-treated group and 5% (=0.20*25%) in the vitamin C group leads to sample sizes of 47 to 59 patients per group [2,3]. Thus, the sample sizes actually calculated by the authors seem to be based on an assumption that vitamin C might decrease AF incidence by 80%, and not by the published assumption of a 20% decrease [1].

Furthermore, those authors observed 7 cases of AF among 52 vitamin C patients and 10 cases of AF among 53 control patients [1]. This leads to a risk ratio (RR) 0.713 that corresponds to 29.7% lower incidence of AF in the vitamin C group. This difference is greater than the 20% effect that was the basis for the sample size calculation by the authors [1], yet the difference was not statistically significant because the number of patients was so small.

Based on a 2014 meta-analysis that included 565 participants [4], and on a 2016 meta-analysis that included 1037 participants [5], there is strong evidence that vitamin C decreases the average risk of AF after cardiac surgery. Therefore, more research on vitamin C and AF is warranted to understand the practical importance of vitamin C and to find out the optimal protocol for its administration. Unfortunately the number of patients in the Antonic et al. trial was so small, and the 95% confidence interval around the observed RR = 0.713 is so wide, that it does not provide substantial additional information of the effects of vitamin C.
References

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https://doi.org/10.1093/icvts/ivu020

https://doi.org/10.15171/apb.2016.033