It is well known that the rate of acute clinically relevant embolic events during peripheral interventions is low, and most of these events can be successfully managed during the index procedure, as shown by the study of Shrikhande and colleagues 1 and Dieter and Najundappa. 2 However, nothing is known about the clinical consequences of initially silent distal embolic events in patients undergoing repetitive redo procedures. In particular, patients at high risk for such redo procedures are the ones who have the highest peri-interventional embolic risk: long lesions, chronic total occlusions, and in-stent reocclusions. For clinicians, it is a well-known phenomenon that peripheral outflow is progressively compromised in stepwise fashion with every additional complex procedure. Notably, the clinical implication of this finding is still uncertain. Considering the low incidence of clinically meaningful consequences of peri-interventional embolic events, it is very unlikely that such a large-scale trial evaluating the clinical benefit of any kind of embolic prevention device will be conducted in the near future. However, as mentioned in our article, 3 there exists other meaningful endpoints that might be significantly affected by the use of protection devices, such as radiation time, amount of contrast potentially affecting renal function in patients with renal insufficiency, and, finally, treatment time, and with this catheterization lab time. We definitely agree with Wu and colleagues that a sufficiently powered, hard endpoint trial is mandatory before the general use of the ECA balloon can be recommended. Nevertheless, everything is a matter of cost: if the cost of an ECA balloon is not significantly higher than a 30-cm-long standard angioplasty balloon, the ECA balloon could be at least considered currently in lesions at high risk for distal embolization.

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Between-Study Variability of Short-term Mortality in Patients With Pararenal Aortic Pathologies Treated With Chimney or Fenestrated Endografts

To the Editors:

In analyses that pool the results from different clinical studies, datasets characterised by numerous zeros in event frequencies are at increased risk of generating spurious results.1-3 In their analysis of 30-day mortality in patients with pararenal aortic pathologies receiving chimney or fenestrated (f-EVAR) endografts, Donas and co-workers4 included a total of 17 clinical studies (5 and 12 for the two types of endografts, respectively), 9 of which had zero events. Another methodological issue with this study is that no heterogeneity assessment was carried out, whereas current guidelines on observational meta-analysis recognize the importance of this
Finally, no details were reported on the methods used for estimating 95% confidence intervals (CI).

We have re-analyzed the 30-day mortality data reported by Donas et al. by using more specific techniques of observational meta-analysis. In particular, the issue of zero frequencies was handled by introducing the Freeman-Tukey transformation that was applied to estimate all 95% CIs for both study-specific and pooled mortality rates. The study-specific mortality rates were weighted according to their standard errors, and heterogeneity was estimated by standard methods; the statistical model was random-effect. Furthermore, the comparison of 30-day mortality between chimney endografts (123 patients from 5 studies) and fenestrated endografts (660 patients from 12 studies) was carried out using meta-regression, which is recognized to be the standard method for generating a statistical comparison. In our meta-regression, 30-day mortality (dependent variable) was handled as a transformed value (according to Freeman and Tukey), while covariates included type of endograft and publication date. A stepwise approach was employed that retained in the model all covariates showing $p < 0.10$. The information needed for our re-analysis was extracted from Tables 1 and 2 of the published article (Note: the sum of the subgroup 2 patients is 660, but Table 2 gives 631, presumably due to a typing error). Both meta-analysis and meta-regression calculations were based on the use of a specific software (Open Meta-Analyzer, version 4.16.12; Tufts University, Boston, MA, USA; available at http://tufоскас.орг/open-meta/).

The pooled rates (Figure) of 30-day mortality resulting from our analysis [5.7% (95% CI 1.4% to 12.7%) vs. 2.4% (95% CI 1.4% to 3.7%) for the chimney and the f-EVAR groups, respectively] were higher than the corresponding rates estimated by Donas et al. [0.58% (95% CI 0% to 2.93%) vs. 1.17% (95% CI 0.26% to 2.09%) for the chimney and the f-EVAR groups, respectively]. These findings seem to confirm the presumably excessive statistical weight that Donas and colleagues have attributed to zero frequencies. According to our results, the degree of heterogeneity of these analyses was quite low. At our meta-regression, no covariate met the criterion for being retained in the model; $p$-values were 0.341 for type of endograft and 0.608 for publication date. The pooled risk difference in 30-day mortality for chimney vs. f-EVAR was $+4.6\%$, but its 95% CI was very wide (from $-4.9\%$ to $+14.0\%$), in keeping with the lack of statistical significance.

In summary, while confirming that 30-day mortality shows no difference between the two devices, our results nonetheless suggest that the pooled rates of this endpoint are higher than the values estimated by Donas et al.; more importantly, according to our results, the 95% CIs for these estimates were much larger than those reported by the German authors. Therefore, no conclusion can be drawn on whether or not these two types of devices have the same degree of effectiveness (as judged by 30-day mortality); in light of our 95% CIs, chimney devices can in fact determine from $-4.9\%$ to $+14\%$ mortality at 30 days as compared with fenestrated ones.
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research findings in the form of the proportion of a sample with a particular characteristic can be represented with the proportion as the effect size statistic with values ranging from 0.0 to 1.00. In our study, the effect size statistic was the proportion of 30-day mortality.

We are glad that the re-analysis from our Italian colleagues showed no difference in 30-day mortality between the chimney and fenestrated technique, which is in accord with our results. However, robust clinical conclusions regarding the two endovascular techniques are very difficult to determine and probably cannot be accurately drawn from any statistical comparison. The indications for chimney and fenestrated endografting are in the majority of the published cases different even if the statistical method used by Maratea and colleagues showed low heterogeneity between the two subgroups. Patients with symptomatic or ruptured aortic pathologies can be treated in the urgent setting only with chimney endografts at the moment. The inclusion of this patient population in the chimney publications may influence the mortality rate significantly; on the other hand, this cannot be illustrated with any statistical analysis. Finally, only clinical experience with chimney endografts will give the answer about the utility and durability of this promising alternative therapeutic modality.

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