

The sequential monitoring of covariate-adaptive randomized clinical trials is standard in modern clinical studies. However, the validity of this sequential procedure is not well studied in the literature. Clinical trialists therefore implement the procedure and perform data analysis based on the theory of the sequential monitoring of fixed designs, which is often incorrect and many clinical trials are open to question. In this paper, we study the theoretical properties of the sequential procedure and propose some important adjustments to classical statistical inference. Under different scenarios, we derive the asymptotic joint distribution of the sequential test statistics. Further, we estimate the decreased variability of the estimated treatment effect due to covariate-adaptive randomization, so that the sequential test statistics can be adjusted to be an asymptotic Brownian motion and the type I error rate can be controlled in real trials. Numerical results from simulation and the redesign of a clinical trial support our theoretical findings, showing that our procedure can control the type I error rate well, and also demonstrating the advantages of our method in terms of power and early stopping. Both theoretical and numerical results provide important guidance for future practical clinical trials using covariate-adaptive randomization procedures.