Application of win ratio methodology in the Global SYMPLICITY Registry for patients with atrial fibrillation or obstructive sleep apnea

F. Mahfoud[1], G. Mancia[2], C. Ukena[1], R. Schmieder[3], K. Narkiewicz[4], L. Ruilope[5], M. Schlaich[6], B. Williams[7], M. Fahy[8], M. Boehm[1]

[1]Saarland University Medical Center, Homburg/Saar, Germany; [2]University of Milan-Bicocca, Milan, Italy; [3]University hospital Erlangen, Erlangen, Germany; [4]Medical University of Gdansk, Gdansk, Poland; [5]Hospital Universitario 12 de Octubre, Madrid, Spain; [6]Royal Perth Hospital, Perth, Australia; [7]University College London, London, United Kingdom; [8]Medtronic, Santa Rosa, United States of America

Funding Acknowledgement: Type of funding sources: Private company. Main funding source(s): Medtronic

Background/Introduction: The win ratio is a new methodology which utilizes multiple hierarchical endpoints to evaluate clinical outcomes in trials. The win ratio may have added benefit in device therapy trials like renal denervation (RDN) where anti-hypertensive medication burden can influence blood pressure (BP) changes.

Purpose: In this analysis, we applied the win ratio to patients in the Global SYMPLICITY Registry (GSR) to quantify potential differences in RDN efficacy according to different comorbidities, specifically atrial fibrillation and obstructive sleep apnea.

Methods: All patients in GSR had an RDN procedure with the Symplicity Flex or Symplicity Spyral catheter. For the win ratio analysis, ambulatory systolic BP (ASBP) measurements, office systolic BP (OSBP) measurements and the number of prescribed anti-hypertensive medications at 6 months were included as hierarchical endpoints. Patients were divided into 1 of 2 groups: with or without atrial fibrillation (AF) at baseline. Each patient was compared with every other patient in the opposing group first according to ASBP to determine "win", "lose" or "tie" with a threshold of 5 mmHg. Then, ties from the ASBP comparison underwent the comparison using OSBP with a threshold of 10 mmHg. Any tie for a pair comparing OSBP resulted in comparison of number of anti-hypertensive medications with a threshold of 1. Comparisons of ASBP and OSBP were adjusted for baseline SBPs by using residuals from a linear regression. The analysis was repeated for patients grouped according to history of obstructive sleep apnea (OSA) at baseline.

Results: In March 2020, 336 patients with AF at baseline and 2,394 patients with no AF were compared in GSR, resulting in 336 x 2394 = 804,384 pairwise comparisons for the win ratio analysis. A total of 285,709 "wins", indicating greater ASBP reduction, OSBP reduction, and/or fewer number of anti-hypertensive medications occurred in the AF group compared to the no AF group. Conversely, 256,511 "losses", meaning greater BP reduction and/or number of medications occurred in the no AF group. The win ratio was thus calculated as 1.11 (95% CI: 0.98, 1.28, p=0.081) indicating similar BP reduction and medication burden after RDN in patients with or without AF in GSR (Figure). Using these methods, the win ratio for patients with and without OSA was calculated to be 0.98 (95% CI: 0.85, 1.13, p=0.81), also indicating similar RDN efficacy regardless of presence of OSA at baseline (Figure). Previously published results of the win ratio analysis of RDN and sham control patients in the SPRYAL HTN-ON MED trial reported a win ratio in favor of RDN of 2.78 (95% CI: 1.58, 5.48, $p<0.001$).

Conclusions: Application of the win ratio methodology to patients in GSR demonstrated similar efficacy of RDN to patients regardless of whether they had comorbidities of atrial fibrillation or obstructive sleep apnea.