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Comparison of cardiac output measurement methods for mortality prediction in pulmonary hypertension

E. Simsek[1], Y. Bayazit[1], E. Demir[1], M. Kayikcioglu[1], S. Nalbantgil[1], N. Mogolkoc[2], L. Can[1], H. Kultursay[1]. *[1]Ege University, Faculty of Medicine, Department of Cardiology, Izmir, Turkey; [2]Ege University, Faculty of Medicine, Department of Pulmonology, Izmir, Turkey*

Right heart catheterization including cardiac output (CO) measurement is essential step in pulmonary hypertension (PH) diagnosis and follows up. There are only small studies to assess the concordance between different CO measurement methods. There is no study comparing these methods for mortality prediction in PH. The aim of this study is to compare the estimated Fick (eFick), Thermodilution (TD) and impedance cardiography (ICG) methods with regard to mortality prediction in PH patients.

Methods: Study included the retrospective analysis of all patients who had undergone right heart catheterization (RHC) for PH from 2008 to2015. Only patients who have CO measurement with at least two different methods were included. NICCOMO device with arterial compliance modulation technique for ICG-CO measurements was used. Three CO techniques were compared with Bland Altman analysis. CO was indexed to body surface area and cardiac index (CI) was used for all mortality analyses. Kaplan-Meier survival analyses and Cox-proportional hazard regression models were used to compare prediction of all-cause mortality of the 3 different CO methods.

Results: 121 patients had 134 RHC including CO measurements by at least 2 different methods. Median (interquartile range) follow up time was 45 (44) months and 56.2% of the patients died during follow up. There were good correlations between eFick and TD (n: 111, $p<0.001$ r: 0.626) and also TD vs. ICG (n: 47, $p<0.001$ r: 0.622). eFick and ICG was moderately correlated (n: 70, $p<0.001$, r: 0.469). The mean difference (bias) between eFick vs. ICG, ICG vs. TD and eFick vs. TD were respectively 0.9 ml/min., -0.7 ml/min. and -0.3 ml/min; however, limits of agreement results were high in Bland-Altman analysis. Three different methods were used in 47 RHC and low eFick CI (<2.2l/min/m^2) was the only significant mortality predictor compared to other 2 methods (Log rank p values for low eFick: 0.003, HR: 3.671, low TD CI: 0.2, low ICG CI: 0.302). Also 111 patients had simultaneous CO measurements with eFick and TD. Low eFick CI was still significant mortality predictor (For low eFick p: 0.003, HR: 2.388 and for low TD CI p: 0.056). Patients were also categorized in four groups based on agreement between eFick CI and TD CI results. (Concordant normal, concordant low and 2 discordant groups: low eFick CI and normal TD CI or normal eFick CI and low TD CI). Mortality was significantly higher in groups including patients with low eFick CI. However there was no statistical difference between concordant normal CI group and normal eFick CI and low TD CI groups (p: 0.329) (Figure 1)

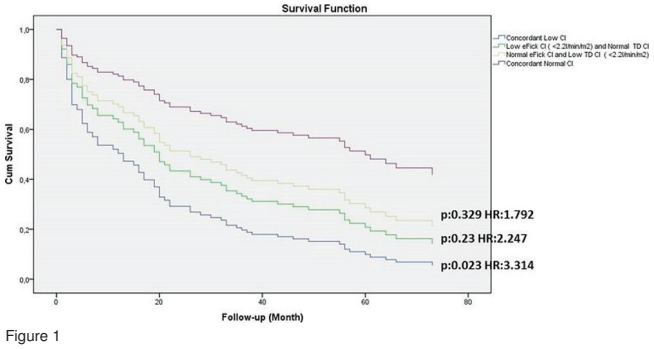

Figure 1

Conclusion: Although, eFick, TD and ICG methods had statistically significant correlations they showed modest agreement in Bland-Altman analyses. eFick CI predicts mortality more accurately than other methods in PH patients. eFick method for CO measurement, should be a standard of care in PH patients.

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Effect of pulmonary arterial hypertension specific therapy in the four clinical subgroups of patients with pulmonary arterial hypertension associated with congenital heart disease

E. Monti, A. Rinaldi, F. Dardi, M. Palazzini, E. Gotti, A. Albini, E. Zuffa, D. Guarino, F. Pasca, A. De Lorenzis, A. Cassani, M. Orzalkiewicz, A. Manes, N. Galie'. *University of Bologna, Department of Specialized, Diagnosticand Experimental Medicine – DIMES - Bologna/IT, Bologna, Italy*

Background: Pulmonary arterial hypertension associated with congenital heart disease (PAH-CHD) is a very heterogeneous disease. There are few published data on the effect of PAH-specific therapy in patients with PAH-CHD and they included only patients with Eisenmenger's syndrome (ES) and PAH after defect correction (DC).

Purpose: The aim of the study was to evaluate the effects of PAH-specific therapy in the 4 clinical subgroups of PAH-CHD patients: ES, PAH associated with prevalent systemic-to-pulmonary shunts, PAH with small/coincidental defects, DC.

Methods: From 1977 to December 2017 consecutive patients with PAH-CHD referred to our centre were included in the study. All patients underwent baseline clinical evaluation, six-minute walking distance (6MWD) and right heart catheterization. The same evaluations were performed before and 3–4 months after the beginning of a new PAH-specific drug initiated in our centre. Changes in 6MWD and haemodynamic parameters were analyzed using Wilcoxon signed-rank test and compared between the 4 clinical subgroups of PAH-CHD patients with Kruskal-Wallis test. Data are presented as median (interquartile range).

Results: 231 consecutive PAH-CHD patients (50% ES, 19% S/P, 6% SD, 25% DC) were enrolled. Patients with complex CHD were excluded from the analysis. Median follow-up was 117 (54–275) months. 102 patients began monotherapy (55 ES, 18 S/P, 7 SD, 22 CS) and 82 patients associated double combination therapy in our centre (44 ES, 10 S/P, 5 SD, 23 CS). Patients who received triple combination therapy were not analyzed because of the small size of the sample. Results are shown in the Table.

Conclusions: Initial monotherapy and double sequential combination therapy were effective in improving haemodynamic profile and exercise capacity in patients with PAH-CHD without any significant difference between the four clinical subgroups.

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Real-world experience with concomitant macitentan and riociguat treatment in patients with pulmonary hypertension (PH) in the OPsumit USers (OPUS) registry

V. McLaughlin[1], K. Chin[2], N. Kim[3], R. Sulica[4], R. Frantz[5], M. Brand[6], E. Muros-Le Rouzic[6], M. Selej[7], R. Channick[8]. *[1]University of Michigan, Division of Cardiovascular Medicine, Ann Arbor, [2]University of Texas Southwestern Medical Center, Department of Internal Medicine, Dallas, [3]University of California San Diego, Division of Pulmonary & Critical Care Medicine, La Jolla, [4]Division Pulmonary, Critical Care and Sleep Medicine, New York University Langone Health, New York, [5]Mayo Clinic, Department of Cardiovascular Medicine, Rochester, United States of America; [6]Actelion Pharmaceuticals Ltd, Global Clinical Science & Epidemiology, Allschwil, Switzerland; [7]Actelion Pharmaceuticals US, Inc, Medical Affairs, South San Francisco, [8]Massachusetts General Hospital, Pulmonary and Critical Care, Boston, United States of America*

Introduction: Data on the use of the endothelin receptor antagonist macitentan and the soluble guanylate cyclase stimulator riociguat to treat pulmonary arterial hypertension (PAH) in combination are limited.

Purpose: OPUS (NCT02126943) provides experience in a real-world setting of the safety of macitentan and riociguat therapy in combination in PH patients.

Methods: OPUS is an ongoing, long-term, prospective, multicentre, observational, drug registry of patients newly treated with macitentan in the US. This analysis includes enrolled patients who received concomitant treatment with macitentan and riociguat. Patient characteristics are described at macitentan initiation. Safety data are described from the time when patients were receiving both macitentan and riociguat and are descriptively compared with data in the overall PH population with follow-up.

Results: As of October 2017, OPUS included 1512 PH patients newly treated with macitentan and with follow-up data; of these, 125 patients were treated concomitantly with riociguat. The reason for macitentan prescription included PAH (n=96, 77%) and chronic thromboembolic PH (CTEPH; n=23, 18%). At macitentan initiation, the median (range) age of the 125 patients was 62.0 (18–88) years and 93 (74%) patients were female. The median (Q1, Q3) exposure to concomitant macitentan and riociguat was 6.3 (2.5, 14.3) months; 34% and 17% of patients had exposures >12 and >18 months. Macitentan was initiated before riociguat in 59 (47%) patients. Adverse events (AEs) experienced during the exposure period are shown in the table.

Abstract P3559 – Table 1

	Pre-Mono	Post-Mono	p-value	p between 4 PAH-CHD clinical subgroups – Mono	Pre-Double	Post-Double	p-value	p between 4 PAH-CHD clinical subgroups – Double
6MWD (m)	403 (340–477)	444 (375–529)	<0.001	0.560	451 (402–549)	489 (426–559)	<0.001	0.922
RAP (mmHg)	7 (5–10)	8 (7–10)	0.062	0.147	9 (6–11)	8 (6–10)	0.472	0.899
mPAP (mmHg)	70 (56–89)	67 (54–83)	<0.001	0.579	74 (60–88)	69 (56–86)	<0.001	0.682
mBP (mmHg)	87 (79–98)	86 (78–94)	0.346	0.214	84 (76–93)	82 (76–90)	0.019	0.600
Pulmonary CI (l/min/m^2)	2.2 (1.6–3.2)	2.7 (2–3.3)	<0.001	0.819	2.4 (1.9–3.1)	2.7 (2.3–3.5)	<0.001	0.792
PVR (W.U.)	17.9 (10.6–24.4)	13.3 (9.9–20.4)	<0.001	0.291	14.5 (11–25.6)	12.7 (8.4–20)	<0.001	0.349
SVR (W.U.)	22.7 (18.4–32.3)	20.8 (16.3–25.3)	<0.001	0.547	20.2 (15.9–25.2)	18.9 (14.7–24)	0.006	0.846

Legend: CI, cardiac index; mBP, mean blood pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; SVR, systemic vascular resistance 6MWD, 6 minute walking distance.