Evaluation of Supracardiac Venous Angioplasty and Stenting on Orthostatic Intolerance and Orthostatic Hypotension - The STANDUP 3 Study

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Background and Significance

Orthostatic hypotension (OH), defined as a systolic blood pressure drop of $\geq$ 20 mmHg or diastolic of $\geq$ 10 mmHg within 3 minutes of standing [1], affects 16–30% of adults aged 65+ (~8.3–15.6 million Medicare beneficiaries in 2023)[2]. OH, a form of orthostatic intolerance (OI), causes dizziness, syncope, and fatigue, increasing risks of mortality, heart disease, stroke[3], atrial fibrillation[4], venous thromboembolism[5], and kidney disease[6]. Current treatments (midodrine, fludrocortisone, droxidopa) are limited by side effects like hypertension[7], urological issues[8], hypokalemia[9], and heart failure[10].

Cerebral vessels integrate fluid drainage [11], with jugular venous valves regulating return [12]. Jugular outflow disturbance contributes to OH [13]. Venous sinus stenosis insights highlight venous roles in neurology [14].

2023 Medicare Part D PUF data show OH drug spending of $86,789,822.21 for ~126,593 patients: Midodrine HCl: 866,382 prescriptions, 106,462 patients, $69,853,535.66, Fludrocortisone Acetate: 232,372 prescriptions, 9,115 patients, $5,824,754.89, Droxidopa (Northera): 724 prescriptions, 16 patients, $11,111,531.66 (incomplete data).

The STANDUP 2 Study hypothesizes that supracardiac venous impairment exacerbates OH/OI by disrupting baroreflex, venous return, and glymphatic clearance[15–17]. The intervention aims to improve regulation and reduce costs.

Specific Aims

1. Assess efficacy in reducing ME and blood pressure drop.
2. Evaluate OHQ score improvements.

Methods

Single-arm registry trial recruiting 200 patients (age $\geq$ 18) with OH/OI at St. Francis Hospital, Roslyn, NY.

- Intervention: Venous angioplasty/stenting with RHC; de-escalate medications (droxidopa $\rightarrow$ pyridostigmine $\rightarrow$ fludrocortisone $\rightarrow$ midodrine).
- Endpoints: Primary (ME/blood pressure); secondary (OHQ).
- Safety: Post-procedure monitoring; DSMB review.
- Analysis: Paired t-tests/ANOVA; power 97.8% (n=200, $p<0.05$).

Potential Benefits and Cost Savings

Intervention may reduce symptoms and medication use. Potential savings: ~$38,950,298.45/year (50% generics, 10% droxidopa reduction). OH-related costs ~$1.0–$2.1B (0.1–0.2% of $1,029.8B Medicare spending).

Limitations

Suppression underestimates patients (96.7% midodrine, 98.9% fludrocortisone, 4.8% droxidopa rows). Droxidopa data incomplete (975 rows). Costs Part D only. Savings hypothetical. Single-center.

Scientific and Public Health Impact

Targets venous outflow for OH/OI, potentially reducing $86.8M Part D burden and $1.0–$2.1B total costs for ~12 million beneficiaries.

2023 OH Drug Costs Table

Drug Name	Prescriptions	Patients	Cost ($)
Midodrine HCl	866,382	106,462	69,853,535.66
Fludrocortisone Acetate	232,372	9,115	5,824,754.89
Droxidopa (Northera)	724	16	11,111,531.66
Total	1,099,478	124,593	86,789,822.21

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