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A New Red Flag Classification to Predict Vasovagal Syncope During Office Hysteroscopy: A Cross-Sectional Pilot Feasibility Study

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Rationale

Office hysteroscopy is increasingly utilized due to advancements in instrumentation and techniques; however, its adoption in routine gynecologic practice remains limited to 10–12% of cases【1,2】. This under utilization is largely attributed to the perception of pain and lack of financial incentives. Consequently, fewer than 20% of gynecologists employ office hysteroscopy for the evaluation of intrauterine pathology【3,4】.

Although generally safe, vasovagal syncope (VVS) is the most concerning complication, with a reported prevalence ranging from 0.21% to 1.85%【5–9】. Other complications include pain, infection, and bleeding【10】. Surgeons often fail to anticipate vasovagal responses during the procedure. This study aims to develop a red flag classification system based on pain response to enable early recognition and prevention of VVS during office hysteroscopy.

Specific Aim

To evaluate the feasibility of a predictive red flag classification system for identifying patients at risk of vasovagal syncope during office hysteroscopy, with the goal of enhancing procedural safety.

Background & Significance

Vasovagal syncope, classified by the European Society of Cardiology as a form of reflex or neurally mediated syncope, is triggered either orthostatically or emotionally—commonly due to fear, pain (somatic or visceral), instrumentation, or blood phobia【11】. It manifests as hypotension, bradycardia, and transient loss of consciousness【12】. Reported incidences vary from 0% to 4%【13–20.

Presyncope or vasovagal reaction is characterized by lightheadedness, palpitations, weakness, nausea, visual disturbances, and sweating. Beyond immediate risks, the consequences include premature procedure termination and increased patient anxiety. Physiologically, VVS is attributed to parasympathetic overactivation, especially during cervical manipulation, leading to a cascade of bradycardia, reduced vascular resistance, hypotension, and cerebral hypoperfusion【21】.

The Bezold–Jarisch reflex further explains VVS pathophysiology, involving baroreceptor-mediated inhibition of sympathetic tone and enhanced vagal activation【22】. Rigid hysteroscopes and the use of CO_2 as a distension medium increase the risk of vasovagal events【23】.

Key risk factors include a prior history of vasovagal reactions, age under 65, and high pre-procedure pain scores【12】. VVS is 1.5 times more common in women, potentially due to physiological differences such as lower body mass index【24,25】.

The proposed classification aims to identify patients with lower pain tolerance likely to experience VVS, enabling timely preventive strategies.

Preliminary Data:

Prof. Sergio Haimovich, Head of Reproductive Surgery at Embriogyn Clinic (Spain), has conducted over 5,000 office hysteroscopies in the past seven years, with only one case of syncope reported, linked to a myocardial infarction in a 75-year-old. This emphasizes the rarity yet potential severity of VVS.

Research design

This is a multicenter, cross-sectional, analytical pilot study enrolling women undergoing office hysteroscopy over 12 months. Ethics approval and informed consent will be obtained at all participating centers.

In office hysteroscopy, we will utilize 1.9–2.9 mm hysteroscopes (primarily Bettocchi type) by the technique of vaginoscopy, without anesthesia or up to level 3a analgesia, in accordance with international consensus recommendations【26】. The choice of distension medium and hysteroscope is left to the operator's discretion. A nurse positioned at the head of the patient will record signs and symptoms of VVR/VVS.

Data Collection

Variables collected:

- Demographics and clinical history (age, sexual active, parity, history of smoking, fasting status, history of dilatation & curettage, menopausal status, comorbid conditions, prior cesarean, prior cervical surgery, prior obstetric trauma (such as severe perineal tears), use of preoperative analgesics, use of preoperative anti-anxiolytics, experience of the surgeon (< 10 yrs or > 10 yrs of practice) is recorded.
- Weight in kilograms, height in meters will be combined to report body mass index (BMI) in kg/m^2. Time Frame: BMI is calculated when the women is enrolled in the study to perform office hysteroscopy.
- Procedure-related factors (hysteroscopy procedure, level of pain management, type/size of instrument, type of fluid media used, use of fluid management system, use of gravity system, i.e. hydrostatic pressure, cervical stenosis, procedure time) is recorded.
- Hemodynamic parameters (pre- and post-procedural blood pressure and pulse) are recorded.
- Vasovagal symptoms and signs (sweating, nausea, hypotension, bradycardia, syncope) are noted during the procedure.
- Tolerance level is recorded post-procedure by an independent nurse (not involved in the hysteroscopy procedure) using the red flag classification. Time Frame: From the initiation of

the office hysteroscopy procedure until the completion of the surgery or the documentation of a vasovagal attack/syncope, assessed for up to 30 minutes.

- Visual analogue score for pain (VAS - P) is independently assessed post procedure by the nurse (not as a part of tolerance score), with zero described as no pain to 10 described a worst possible pain. Time Frame: From the initiation of the office hysteroscopy procedure until the completion of the surgery or the documentation of a vasovagal attack/syncope, assessed for up to 30 minutes.

Routine intraoperative blood pressure/pulse will not be recorded to avoid patient distress that may artificially trigger VVS.

Clinical symptoms include excessive sweating, feeling of warmth, nausea, malaise, weakness, abdominal cramps, hyperventilation, and lightheadedness. Clinical signs include systolic blood pressure < 80 mm Hg and pulse rate < 60 bpm, facial pallor, and loss of consciousness.

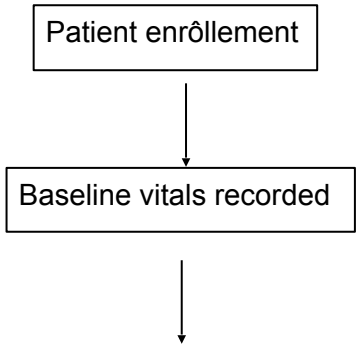
Red Flag Classification

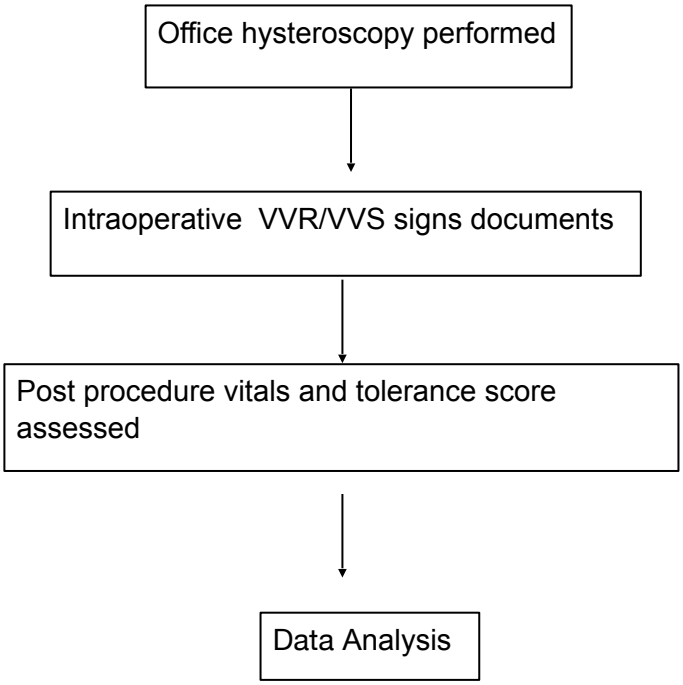
Level	Description	Classification
0	Pain ≤ normal menstruation (Well tolerated)	Green Flag
1	Pain > menstruation, no signs of distress (Tolerated)	Green Flag
2	Level 1 + objective signs (sweating, pallor, malaise) (Tolerated)	Red Flag
3	Level 2 + facial pallor ± loss of consciousness (Not tolerated)	Red Flag

Normal menstruation is when the pain during periods does not interfere with daily activities. The level of pain tolerated by the women in relation to the menstruation is described as a green flag indicating well tolerated or tolerated, or red flag indicating not tolerated.

Note: Patient request to stop the procedure at any level = Red Flag.

Flowchart





Inclusion Criteria

- Women ≥18 years
- Prior gynecological care
- Informed consent provided

Exclusion Criteria

- Inability to consent
- Psychiatric disorders or anxiolytic use
- Use of dilators or anesthesia above level 3a
- Family history of VVS

Sample Size Calculation

Based on an estimated VVS rate of 6.3%【27】, and using a 95% confidence interval, the sample size of 46 was calculated using Crutzen's online tool【28】.

Statistical Analysis

Descriptive analysis will be conducted for continuous and categorical variables. Chi-square tests will evaluate the association between pain classification and vasovagal events. The STROBE checklist will guide reporting.

Primary Outcome

To assess feasibility in implementing the red flag classification system, as preparation for a future large-scale validation study.

Secondary outcome

Potential barriers in implementing the red flag classification system, as preparation for a future large-scale validation study

Pre- specified outcome

To measure visual analogue score for pain post procedure separately from the tolerance score.

To measure the body mass index of participant undergoing office hysteroscopy.

References

1. Urman, Richard D, et al. "Office-Based Surgical and Medical Procedures: Educational Gaps." *PubMed*, vol. 12, no. 4, 1 Jan. 2012.
2. Salazar, Christina Alicia, and Keith B. Isaacson. "Office Operative Hysteroscopy: An Update." *Journal of Minimally Invasive Gynecology*, vol. 25, no. 2, Feb. 2018, pp. 199–208, https://doi.org/10.1016/j.jmig.2017.08.009. Accessed 11 July 2019.
3. Isaacson, Keith. "Office Hysteroscopy: A Valuable but Under-Utilized Technique." *Current Opinion in Obstetrics and Gynecology*, vol. 14, no. 4, Aug. 2002, pp. 381–385, https://doi.org/10.1097/00001703-200208000-00004. Accessed 17 Nov. 2019.
4. Munro, Malcolm G., et al. "Office versus Institutional Operative Hysteroscopy: An Economic Model." *Journal of Minimally Invasive Gynecology*, vol. 29, no. 4, Apr. 2022, pp. 535–548, https://doi.org/10.1016/j.jmig.2021.12.008. Accessed 20 May 2025.
5. Radvansky, Brian M., et al. "In-Office Vasovagal Response after Rhinologic Manipulation." *International Forum of Allergy & Rhinology*, vol. 3, no. 6, 28 Nov. 2012, pp. 510–514, https://doi.org/10.1002/alr.21121. Accessed 25 July 2020.
6. He, Yanni, et al. "First Experience Using 4-Dimensional Hysterosalpingo-Contrast Sonography with SonoVue for Assessing Fallopian Tube Patency." *Journal of Ultrasound in Medicine*, vol. 32, no. 7, 1 July 2013, pp. 1233–1243, https://doi.org/10.7863/ultra.32.7.1233. Accessed 20 Apr. 2023.
7. Ma, Tony, et al. "Is Outpatient Hysteroscopy the New Gold Standard? Results from an 11 Year Prospective Observational Study." *Australian and New Zealand Journal of Obstetrics and Gynaecology*, vol. 57, no. 1, 15 Nov. 2016, pp. 74–80, https://doi.org/10.1111/ajo.12560.
8. Carin, A.-J., and O. Garbin. "Retrait Des Dispositifs Intra-Utérins Sous Hystéroscopie En Consultation : à Propos de 36 Cas." *Journal de Gynécologie Obstétrique et Biologie de La Reproduction*, vol. 44, no. 7, Sept. 2015, pp. 653–657, https://doi.org/10.1016/j.jgyn.2014.09.005. Accessed 20 May 2025.
9. Lo, KW, and Pong Mo Yuen. "The Role of Outpatient Diagnostic Hysteroscopy in Identifying Anatomic Pathology and Histopathology in the Endometrial Cavity." *Journal of the American Association of Gynecologic Laparoscopists*, vol. 7, no. 3, 1 Aug. 2000, pp. 381–385, https://doi.org/10.1016/s1074-3804(05)60482-3. Accessed 25 Oct. 2023.
10. C. Yang, Linda, and Angela Chaudhari. "The Use of Hysteroscopy for the Diagnosis and Treatment of Intrauterine Pathology." *Www.acog.org*, Mar. 2020, www.acog.org/clinical/

clinical-guidance/committee-opinion/articles/2020/03/the-use-of-hysteroscopy-for-the-diagnosis-and-treatment-of-intrauterine-pathology.
11. Brignole, Michele, et al. “2018 ESC Guidelines for the Diagnosis and Management of Syncope.” *European Heart Journal*, vol. 39, no. 21, 19 Mar. 2018, pp. 1883–1948, academic.oup.com/eurheartj/article/39/21/1883/4939241, https://doi.org/10.1093/eurheartj/ehy037.
12. SUN, LIPING, et al. “Prophylactic Atropine Administration Prevents Vasovagal Response Induced by Cryoballoon Ablation in Patients with Atrial Fibrillation.” *Pacing and Clinical Electrophysiology*, vol. 40, no. 5, 25 Apr. 2017, pp. 551–558, https://doi.org/10.1111/pace.13072. Accessed 12 Jan. 2022.
13. Kennedy, David J, et al. “The Use of Moderate Sedation for the Secondary Prevention of Adverse Vasovagal Reactions.” *Pain Medicine (Malden, Mass.)*, vol. 16, no. 4, Apr. 2015, pp. 673–9, pubmed.ncbi.nlm.nih.gov/25529469/, https://doi.org/10.1111/pme.12632.
14. Abbasi, Arjang, et al. “Complications of Interlaminar Cervical Epidural Steroid Injections.” *Spine*, vol. 32, no. 19, Sept. 2007, pp. 2144–2151, https://doi.org/10.1097/brs.0b013e318145a360. Accessed 14 June 2022.
15. Kennedy, David J., et al. “Vasovagal Rates in Flouroscopically Guided Interventional Procedures: A Study of over 8,000 Injections.” *Pain Medicine*, vol. 14, no. 12, Dec. 2013, pp. 1854–1859, https://doi.org/10.1111/pme.12241. Accessed 18 Aug. 2021.
16. Diehn, Felix E, et al. “An Audit of Transforaminal Epidural Steroid Injections without Sedation: Low Patient Dissatisfaction and Low Vasovagal Rates.” *Pain Medicine*, vol. 14, no. 7, 16 Apr. 2013, pp. 994–998, https://doi.org/10.1111/pme.12092. Accessed 28 Apr. 2025.
17. Botwin, Kenneth P, et al. “Complications of Fluoroscopically Guided Interlaminar Cervical Epidural Injections.” *Archives of Physical Medicine and Rehabilitation*, vol. 84, no. 5, May 2003, pp. 627–633, https://doi.org/10.1016/s0003-9993(02)04862-1. Accessed 26 Dec. 2022.
18. Trentman, Terrence L., et al. “Vasovagal Reactions and Other Complications of Cervical vs. Lumbar Translaminar Epidural Steroid Injections.” *Pain Practice*, vol. 9, no. 1, Jan. 2009, pp. 59–64, https://doi.org/10.1111/j.1533-2500.2008.00242.x. Accessed 29 Dec. 2022.
19. Carr, Carrie M, et al. “Immediate Adverse Events in Interventional Pain Procedures: A Multi-Institutional Study.” *Pain Medicine (Malden, Mass.)*, vol. 17, no. 12, Dec. 2016, pp. 2155–2161, pubmed.ncbi.nlm.nih.gov/28025351/, https://doi.org/10.1093/pm/pnw051.
20. Vidri, Ron, et al. “Managing Vasovagal Reactions in the Outpatient Pain Clinic Setting: A Review for Pain Medicine Physicians Not Trained in Anesthesiology.” *Pain Medicine*, vol. 23, no. 6, 18 Dec. 2021, pp. 1189–1193, pmc.ncbi.nlm.nih.gov/articles/PMC11009683/, https://doi.org/10.1093/pm/pnab345.
21. Sheldon, Robert S., et al. “2015 Heart Rhythm Society Expert Consensus Statement on the Diagnosis and Treatment of Postural Tachycardia Syndrome, Inappropriate Sinus Tachycardia, and Vasovagal Syncope.” *Heart Rhythm*, vol. 12, no. 6, June 2015, pp. e41–e63, mayoclinic.pure.elsevier.com/en/publications/2015-heart-rhythm-society-expert-consensus-statement-on-the-diagn, https://doi.org/10.1016/j.hrthm.2015.03.029.
22. Fenton, Alexis M. “Vasovagal Syncope.” *Annals of Internal Medicine*, vol. 133, no. 9, 7 Nov. 2000, p. 714, https://doi.org/10.7326/0003-4819-133-9-200011070-00014. Accessed 15 Apr. 2020.
23. Agostini, Aubert, et al. “Risk of Vasovagal Syndrome during Outpatient Hysteroscopy.” *The Journal of the American Association of Gynecologic Laparoscopists*, vol. 11, no. 2, 1 May 2004, pp. 245–247, https://doi.org/10.1016/s1074-3804(05)60207-1.
24. A, Abbasnezhad , et al. The Incidence Rate of Vasovagal Reactions and Its Effective Factors among Blood Donors in Mashhad Blood Transfusion Centers. 23 July 2018.

25. Ghariq, Maryam, et al. “A Higher Proportion of Men than of Women Fainted in the Phase without Nitroglycerin in Tilt-Induced Vasovagal Syncope.” *Clinical Autonomic Research : Official Journal of the Clinical Autonomic Research Society*, vol. 30, no. 5, Oct. 2020, pp. 441–447, pubmed.ncbi.nlm.nih.gov/31953616/, https://doi.org/10.1007/s10286-020-00666-5.
26. Carugno, J, et al. “International Consensus Statement for Recommended Terminology Describing Hysteroscopic Procedures.” *Facts, Views and Vision in ObGyn*, vol. 13, no. 4, Oct. 2021, pp. 287–294, https://doi.org/10.52054/fvvo.13.4.037. Accessed 17 Feb. 2022.
27. Úbeda, A, et al. “Predictors of Vasovagal Symptoms or Syncope during Outpatient Diagnostic Hysteroscopy: A Prospective Observational Study.” *European Journal of Obstetrics, Gynecology, and Reproductive Biology*, vol. 309, May 2025, pp. 121–125, pubmed.ncbi.nlm.nih.gov/40121697/, https://doi.org/10.1016/j.ejogrb.2025.03.044.
28. Viechtbauer, Wolfgang, et al. “A Simple Formula for the Calculation of Sample Size in Pilot Studies.” *Journal of Clinical Epidemiology*, vol. 68, no. 11, Nov. 2015, pp. 1375–1379, www.sciencedirect.com/science/article/pii/S0895435615003030, https://doi.org/10.1016/j.jclinepi.2015.04.014. Accessed 19 Mar. 2019.