

The Impact of the VEGA-1 trial on local hospital providers' first line vasopressor use

Christopher Ansay, Nick Fong, Elizabeth Whitlock, Rishi Kothari, Matthieu Legrand, Michael P. Bokoch

University of California, San Francisco, School of Medicine; Department of Anesthesiology and Perioperative Care, University of California, San Francisco; Department of Anesthesiology & Perioperative Medicine, Thomas Jefferson University

Background

Hypotension can occur during surgery which causes decreased blood perfusion to vital organs and increases morbidity and mortality. Treating hypotension adequately with vasopressors may improve long-term outcomes for patients.¹ Norepinephrine (NE) and phenylephrine (PE) are the two vasopressors most commonly used in the perioperative setting to treat hypotension.² PE is an alpha-1 adrenergic agonist that causes vasoconstriction. NE is an alpha and beta-adrenergic agonist that causes vasoconstriction and increased contractility.³ The VEGA-1 trial was a pilot cluster randomized crossover study at five hospitals that established the feasibility of implementing a much larger clinical trial that will study patient outcomes when using either NE or PE for prevention and treatment of intraoperative hypotension during major surgery under general anesthesia⁴. Before VEGA-1, PE was the most predominantly used vasopressor for major non-cardiac surgeries at UCSF.

The VEGA-1 trial ran from July-December 2021 and successfully randomized patients to a specific vasopressor using a cluster-randomized, multiple crossover design. During VEGA-1, patients were randomized to either NE or PE as the first line infusion each month at each hospital. VEGA-1 showed that NE infusion was safe, but the trial was not powered to detect a difference in postoperative outcomes. VEGA-1 provides an opportunity to study long-term effects of this pragmatic trial on local anesthesia practice at UCSF.

Objective

We aim to determine if the VEGA-1 trial changed local practice and established equipoise between NE and PE as first-line vasopressor infusions. We hypothesize that the VEGA-1 trial increased NE use in major surgery under general anesthesia at UCSF.

VEGA Vasopressor	Period A	Period B	Total
Phenylephrine cases	2772 (87.7%)	2004 (72.3%)	4776 (80.5%)
Norepinephrine cases	388 (12.3%)	769 (27.7%)	1157 (19.5%)

• **Period A: 6 months before VEGA-1**

• **Period B: 6 months after VEGA-1**

Table 1. Proportion of eligible cases receiving either PE or NE as first line during Period A and Period B.

Methods

This is a retrospective cohort study at three UCSF hospitals from January 2021-May 2023. Data from non-UCSF hospitals participating in VEGA-1 was not available. Time period A is defined as the 6 continuous months before VEGA-1. Period B is defined as the 6 months after VEGA-1. The inclusion criteria are age ≥ 18 , inpatient admission, and surgery > 2 hours under general anesthesia. The exclusion criteria are cardiac, transplant, and obstetric surgeries. The primary outcome is the proportion of eligible cases receiving NE as 1st-line vasopressor. Deidentified patient data including surgery type, service, medical history, intraoperative medications, and laboratory values was extracted from the electronic record. The primary outcome was compared for Period A and B using Chi-square. Interrupted time-series analysis was used to compare trends before and after VEGA-1. The secondary outcome (% of patients in eligible cases that have an AKI post-op) will be analyzed using Chi-square. Statistical analyses were run in Stata.

Results

5933 cases were analyzed, with 12.3% NE use in Period A and 27.7% NE use in Period B (Table 1). The proportion of NE use differed by period, $p < .0001$. In all hospitals, baseline NE use was 11.7% and did not change significantly during Period A (slope = 0%/month, 95%CI, -0.2 to 0.6). At the start of Period B, there was an immediate 11% (95% CI, 7.8 to 14.6) increase in NE use. After VEGA-1, NE use increased linearly by 1.4%/month [95%CI, 1.1-1.8]. As of the most recent follow up, 17 months after VEGA-1, the strong linear trend continued with no plateau in NE use. When looking at NE use by hospital, all three hospitals showed a linear trend towards increased NE in the 16 months following the VEGA-1 trial. Mission Bay NE use increased linearly by 0.7%/month [95%CI, 0.1 to 1.5]. Moffitt NE use increased linearly by 1.8%/month [95%CI, 1.3-2.2]. Mt. Zion NE use increased linearly by 1.0%/month but was not significant [95%CI, -0.1-2.1].

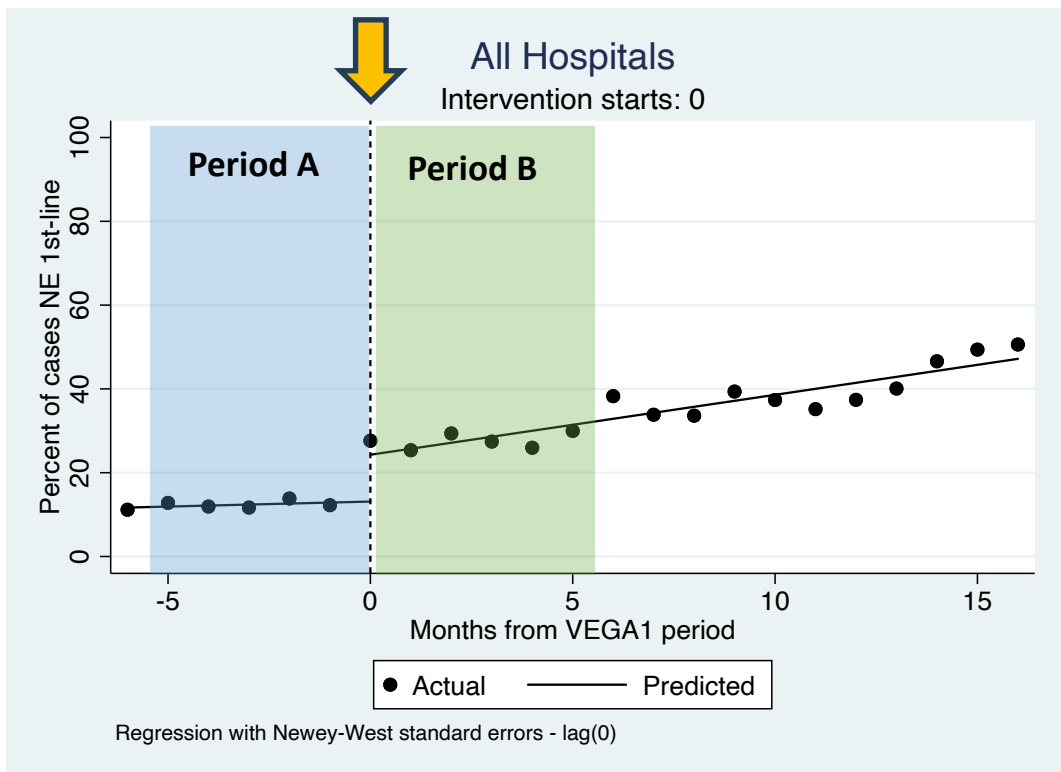


Fig. 1 Trends in NE use before and after VEGA-1 for all three hospitals combined (Interrupted time-series analysis). Yellow arrow represents the VEGA-1 trial period (six months).

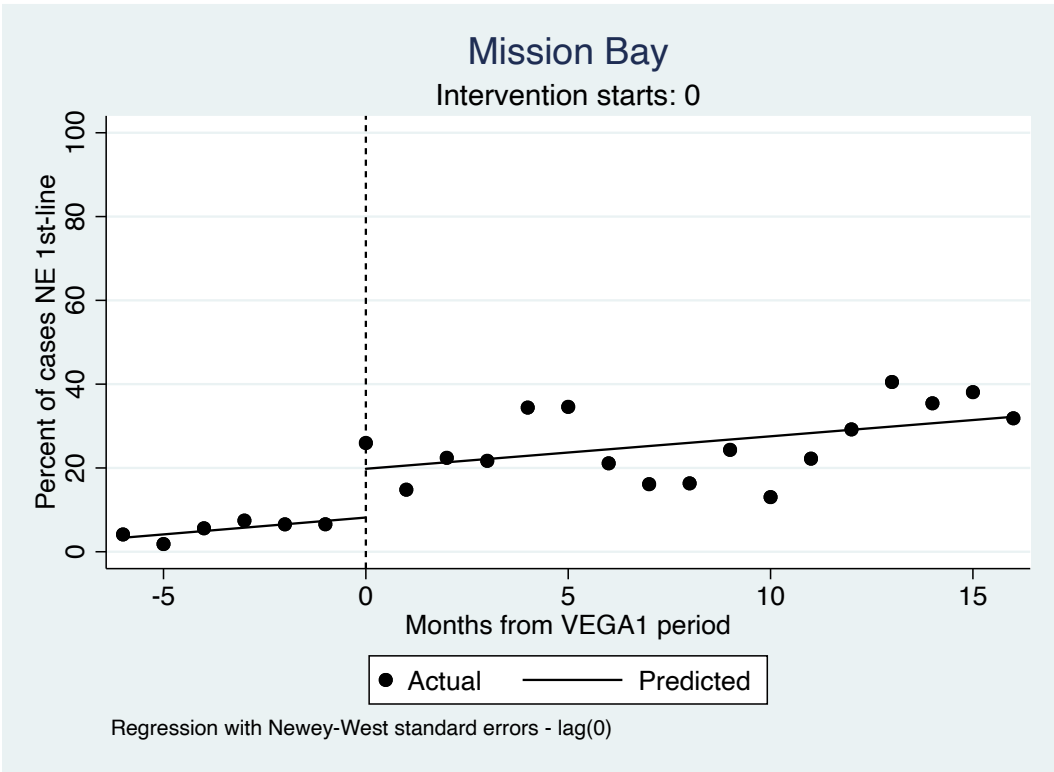


Fig. 2 Trends in NE use before and after VEGA-1 for Mission Bay (Interrupted time-series analysis).

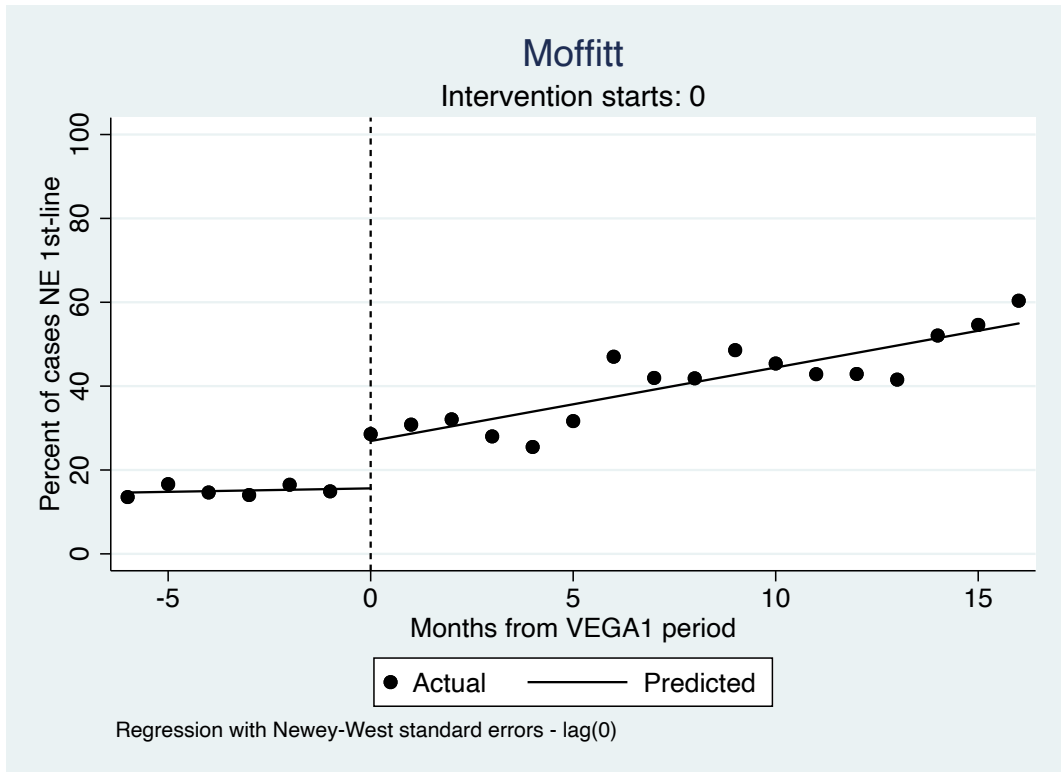


Fig. 3 Trends in NE use before and after VEGA-1 for Moffitt (Interrupted time-series analysis).

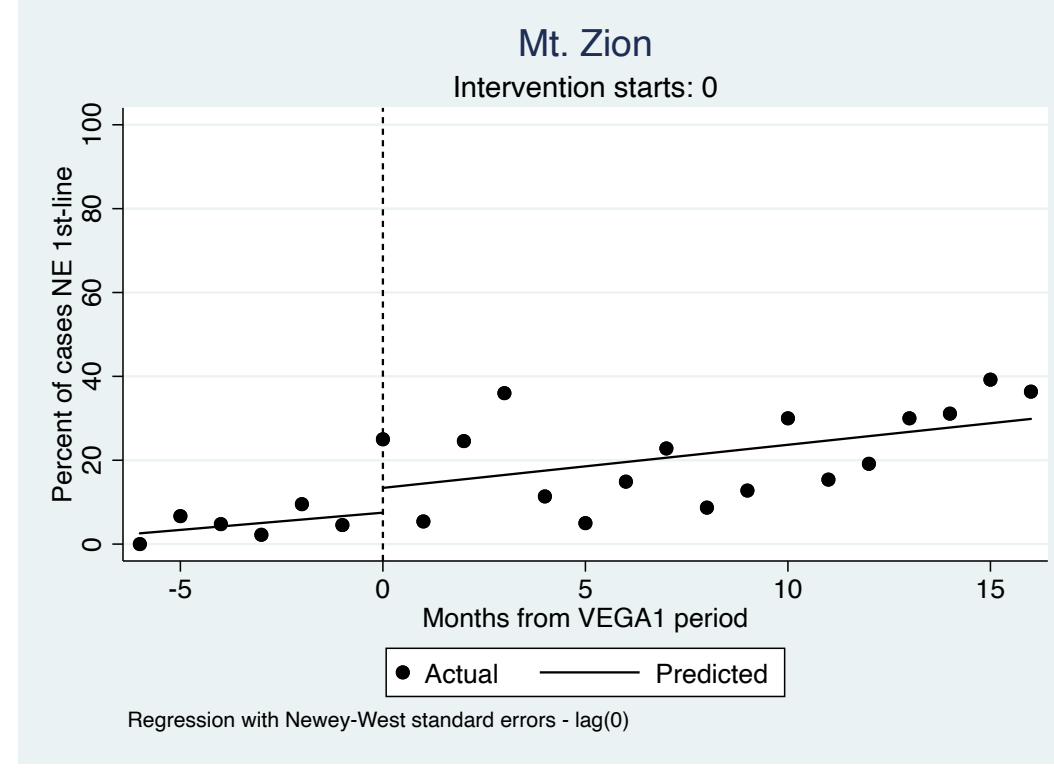


Fig. 4 Trends in NE use before and after VEGA-1 for Mt. Zion (Interrupted time-series analysis).

Conclusions

Norepinephrine use at UCSF had immediate increases following the end of the VEGA-1 trial. During the 16 months of follow-up, each hospital displayed a positive linear increase over time. When separating findings by hospital, Mt. Zion NE use did show a linear increase but was not significantly positive. This is likely due to multiple factors such as case numbers over time or types of surgeries at the hospital. Overall, there is promising data that clinical practice is governed by evidence-based practice. It is possible that large pragmatic clinical trials can create long term changes on clinical practice depending on protocols and findings. With the VEGA-1 trial showing NE's safety, it has helped local clinical practice accept equipoise between the two vasopressors. Next steps will include analyzing the impact on acute kidney injury during this time period.

References

- Sessler DI, Bloomstone JA, Aronson S, et al. Perioperative Quality Initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery. *Br J Anaesth.* 2019;122(5):563-574. doi:10.1016/j.bja.2019.01.013
- Chiu C, Fong N, Lazzareschi D, et al. Fluids, vasopressors, and acute kidney injury after major abdominal surgery between 2015 and 2019: a multicentre retrospective analysis. *Br J Anaesth.* 2022;129(3):317-326. doi:10.1016/j.bja.2022.05.002
- Legrand M, Zarbock A. Ten tips to optimize vasopressors use in the critically ill patient with hypotension. *Intensive Care Med.* 2022;48(6):736-739. doi:10.1007/s00134-022-06708-y
- Legrand M, Kothari R, Fong N, Palaniappa N, Boldt D, Chen LL, Kurien P, Gabel E, Sturgess-DaPrato J, Harhay MO, Pirracchio R, Bokoch MP; VEGA-1 trial investigators. Norepinephrine versus phenylephrine for treating hypotension during general anaesthesia in adult patients undergoing major noncardiac surgery: a multicentre, open-label, cluster-randomised, crossover, feasibility, and pilot trial. *Br J Anaesth.* 2023 Mar 14:S0007-0912(23)00062-4. doi: 10.1016/j.bja.2023.02.004. Epub ahead of print. PMID: 36925330.

Acknowledgments

We would like to acknowledge the UCSF School of Medicine Deep Explore Program. MB acknowledges funding from the UCSF Dept. of Anesthesia & Perioperative Care.