Baxter

Starling
FLUID MANAGEMENT
MONITORING SYSTEM

STARLING AND FLUID MANAGEMENT PUBLISHED STUDIES

OVER 100 PEER-REVIEWED STARLING PUBLICATIONS

– Multiple clinical settings (ICU/OR/ED/Exercise Lab/Outpatient)
– Comparative analyses against all major technologies, including Swan Ganz, Pulse Contour, Doppler and Fick

STARLING VALIDATION

The Starling system is the only non-invasive monitor that has been successfully compared to thermodilution in multiple clinical settings.

Rich J, et al. Noninvasive cardiac output measurements in patients with pulmonary hypertension. *Eur Respir J.* 2013;42:125-33. Study limitations: Single-site, nonrandomized, small study	- 50 consecutive patients with pulmonary hypertension receiving a right-heart catheterization were also monitored with the **Starling** system and indirect Fick. - The study showed that the **Starling** system had improved accuracy and precision over thermodilution when both devices were compared to Fick. - The **Starling** system accurately detected directional changes to a vasoactive medication administration.
Heerdt PM, et al. Noninvasive cardiac output monitoring with bioreactance as an alternative to invasive instrumentation for preclinical drug evaluation in beagles. *J Pharmacol Toxicol Methods*. 2011;64:111-18. Study limitations: Animal study; did not use human subjects	- The **Starling** algorithm was compared to an aortic flow probe in beagles. Aortic flow probe is the gold standard in measuring blood flow. - In over 516 distinct measurements, the **Starling** system exhibited a high degree of accuracy and precision when compared with the aortic flow probe. - This study also highlights the algorithm's ability to handle low flow states: • Accuracy compared to flow probe: **Starling** system 95% • Precision (bias) compared to flow probe: **Starling** system 6.1% vs. flow probe 0.8% • Sufficient fidelity to detect and quantify acute, drug-induced, directional changes in CO

FLUID MATTERS

Because IV fluids do not always help hemodynamically unstable patients and can even cause harm, it is critical to accurately predict patient fluid responsiveness in order to optimize treatment.

Bentzer P, et al. Will this hemodynamically unstable patient respond to a bolus of intravenous fluids? *JAMA*. 2016;316:1298-309. Study limitations: Meta-analysis of single-center studies; did not include randomized controlled studies	- Meta-analysis evaluating over 50 studies (2,260 patients), looking at tests to predict fluid responsiveness. This is the largest fluid responsiveness analysis to date. It did not include the **Starling** system. - Summary fluid responsiveness is 50% (95% CI 42% to 56%). The study evaluates physical exam, CVP, pulse pressure variation, IVCc, echo, cardiac output/stroke volume to assess fluid responsiveness. - Physical exam and CVP cannot be used to reliably predict fluid responsiveness. - Pulse pressure, SV variation, IVCc work in very limited clinical conditions (require controlled ventilation). - SV change was the best predictor of fluid effectiveness (sensitivity 88%, specificity 92%).
Marik PE, et al. Fluid administration in severe sepsis and septic shock, patterns and outcomes: an analysis of a large national database. *Intensive Care Med*. 2017;43(5):625-32. Study limitations: Hospital administration database; some limitations to data set, such as not having physiological data	- In this Premier database analysis, 23,513 patients with severe sepsis and septic shock were admitted to the ICU from the ED. - Day 1 fluid averaged 4.4 L, and for each liter over 5 L, mortality increased by 2.3%, and added $999 treatment cost. - Even the small difference of 600 cc can increase the patient's risk.

ASSESSING FLUID RESPONSIVENESS WITH THE STARLING FLUID MANAGEMENT MONITORING SYSTEM

Marik PE, et al. The use of bioreactance and carotid Doppler to determine volume responsiveness and blood flow redistribution following passive leg raising in hemodynamically unstable patients. *Chest*. 2013; 143(2):364-70. Study limitations: Small single-center study	- The study demonstrated that a passive leg raise (PLR) maneuver using the **Starling** system provides an accurate method of assessing volume responsiveness in critically ill patients. - PLR results (SV>10%=fluid responsive) were compared to carotid Doppler in 34 hemodynamically unstable patients. - The PLR maneuver had a sensitivity of 94% and a specificity of 100% for predicting volume responsiveness (one false negative). - The **Starling** system is the only non-invasive technology with a validation study evaluated during the PLR.

CLINICAL AND FINANCIAL OUTCOMES WITH THE STARLING FLUID MANAGEMENT MONITORING SYSTEM

As demonstrated in the recently published FRESH prospective multi-center randomized clinical trial and an earlier outcome study, stroke-volume-guided resuscitation using dynamic assessment of fluid responsiveness and the Starling system may lead to better outcomes in sepsis patients and reduced costs of care.

Douglas IS, et al. Fluid response evaluation in sepsis hypotension and shock: a randomized clinical trial. *Chest*. 2020;158(4):1431-1445.

Study limitations: Unblinded usual care arm; study not powered to detect differences in all sepsis-associated organ dysfunctions or patient deaths

- First prospective multi-center randomized clinical trial (124 patients at 13 hospitals in the United States and the United Kingdom) to evaluate the efficacy of using dynamic measures (stroke volume change during passive leg raise, or PLR), before administering any clinically driven fluid bolus or increase in vasopressors, to guide resuscitation of sepsis patients (83 in intervention arm and 41 in usual care arm).
- The study demonstrated improved outcomes when a dynamic assessment of fluid responsiveness via PLR was used to guide treatment in severe sepsis and septic shock patients.
  - Decreased fluid balance (1.37 L)
  - Reduced risk of mechanical ventilation (48%)
  - Reduced risk of renal replacement therapy (71%)
  - More likely to be discharged home alive (20%)
- The results of this study are consistent with those of the 2017 University of Kansas study summarized below.

FRESH Prospective Multi-Center Randomized Clinical Trial				
	Variable	SV Guided	Control	Δ/*P* Value*
Primary Endpoint	Fluid Balance (Liters)	0.65 ± 2.85 L	2.02 ± 3.44 L	1.37 L *P* = 0.021*
Secondary Endpoints	Initiation of Renal Replacement Therapy (Relative Risk)	5.1%	17.5%	RRR = 71% *P* = 0.042*
	Initiation of Mechanical Ventilation (Relative Risk)	17.7%	34.1%	RRR = 48% *P* = 0.04*
	ICU LOS (Days)	3.31 ± 3.51	6.22 ± 10.72	2.91 days *P* = 0.113
	Ventilator Use (Hours)	46.99 ± 52.33	119.42 ± 134.9	72 hours *P* = 0.079
	Pressor Use (Hours)	40.74 ± 51.23	55.64 ± 87.42	15 hours *P* = 0.426
	Change in Serum Creatinine	0.13	0.04	0.09 *P* = 0.45
Exploratory Endpoints	Discharged Home Alive	63.9%	43.9%	20% *P* = 0.035**
	30-Day Mortality	15.7%	22%	6.3% *P* = 0.388

* *P* value < 0.05 demonstrates statistical significance
** Not included in formal statistical testing

CLINICAL AND FINANCIAL OUTCOMES WITH THE STARLING FLUID MANAGEMENT MONITORING SYSTEM (Continued)

Latham H, et al. Stroke volume guided resuscitation in severe sepsis and septic shock improves outcomes. *J Crit Care.* 2017;28:42-46.

Study limitations: Retrospective matched, single-center study

- Retrospective matched, single-center study, SV group comprised 100 patients, with 91 patients in the usual care group.
- The study demonstrated that implementing SV-guided resuscitation in patients with severe sepsis and septic shock was associated with improved patient outcomes.
  - Reduced fluid balance and reduced time on pressors
  - Reduced length of stay (2.89 days)
  - Decreased need for mechanical ventilation (25%) and acute dialysis (13.25%)

University of Kansas Retrospective Matched, Single-Center Study					
Variable	Starling Stroke Volume Fluid Therapy (n=100)[1]	Usual Care (Control, n=91)[1]	Δ/*P* Value[1]	Costs Assumptions*	Cost Avoidance*[2]
ICU LOS (Days)	5.98 ± 0.68	8.87 ± 1.18	2.89 days *P* = 0.03	$4,004/ICU day[3] $906/floor day[4]	$8,953
Fluid Balance (Liters)	1.77 L ± 0.60	5.36 L ± 1.01	3.59 L *P* = 0.002		
Pressor Use (Hours)	32.08 ± 5.22	64.86 ± 8.39	32.78 hours *P* = 0.001		
Mechanical Ventilation (Relative Risk)	29%	57%	RR = 0.51 *P* = 0.0001	$1,522/day[5] 5.1 days[4]	$1,940
Acute Dialysis Therapy Initiated	6.25%	19.5%	RR = 0.68 *P* = 0.01	$27,182 x (lc) (12.73 cases avoided/ 96 total patients)[4]	$3,605
ESTIMATED SAVINGS PER TREATED PATIENT*					**$14,498**

*Based upon supplemental data.

COST ASSUMPTIONS

ICU Length of Stay (LOS): 2.89 days x ($4,004 [Avg ICU Day] – $906 [Avg Floor Day]) = $8,953

Mechanical Ventilation (MV): $1,522 x 5.1 days x .25 = $1,940

Assumes:

1. Incremental cost of MV $1,522/day. 2. Average duration of MV in septic shock 5.1 days. 3. An absolute 25% reduction of patients receiving mechanical ventilation.

Acute Dialysis Therapy: $27,182 (avg. dialysis-related hospital costs) x (12.73 cases avoided/96 total patients) = $3,605

REFERENCES

1. Latham H, Bengtson C, Satterwhite L, et al. Stroke volume guided resuscitation in severe sepsis and septic shock improves outcomes. *J Crit Care.* 2017;28:42-46.
2. Latham H, Bengtson C, Satterwhite L, et al. Sepsis resuscitation based on stroke volume optimization improves outcome and reduces cost of care. *Crit Care Med.* 2018; 46:709.
3. Huynh T, Kleerup E, Wiley J, et al. The frequency and cost of treatment perceived to be futile in critical care. *JAMA Inter Med.* 2013;173(20):1887-94.
4. Premier Data Set, 2013. Premier, Inc.
5. Dasta JF, McLaughlin TP, Mody SH, Piech CT. Daily cost of an intensive care unit day: The contribution of mechanical ventilation. *Crit Care Med.* 2005;33(6):1266-1271.

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