

Vascular Access Flow: Are NephroFlow & Transonic HD03 Hemodialysis Monitor Measurements Interchangeable?

Cornelis J Drost & Nikolai Krivitski D.Sc., PhD

Translation of article: "Blutfluss im Gefäßzugang: Sind die Messungen des NephroFlow- und des Transonic-HD03-Hämodialysemonitors austauschbar?" Spektr Dial Apher 2017; 07(1): 42-44

Since its introduction in 1995¹ three generations of Transonic Hemodialysis Patient Monitors (HD01, HD02, HD03) have been validated in multiple animal, MRI, bench and patient studies. Also, millions of measurements in patients each year have established ultrasound indicator dilution technology, as implemented in the Transonic HD Monitors, as the undisputed Gold Standard for vascular access flow measurements. All current USA, Canadian, European, and Asia-Pacific hemodialysis patient flow surveillance guidelines are based on the more than 200 publications from around the world by clinicians using Transonic ultrasound dilution HD Monitors.

Introduction

Holger Böckler (D.Med Consulting AG, a Nipro D.Med division) presents, in a recent German article², the results of a comparison between 79 NephroFlow and HD03 access flow measurements from 34 patients in two clinics. No names of clinics or doctors were provided.

The comparison includes a Bland Altman plot (ibid, Abb.6), unusually formatted with a logarithmic scale that obscures the large variability between the two devices. No statistical data analysis is provided: Mr. Böckler only provides a qualitative discussion (ibid, p. 29) to support his conclusion that the Nipro D.Med NephroFlow device may be used as a substitute for the Transonic HD03 Monitor for patient access flow surveillance.

To our knowledge and contrary to accepted medical device safety and efficacy requirements,

no independent user validation (absolute or comparative) of the NephroFlow device has been published to date. This Böckler report is the first test of NephroFlow's access flow measurement accuracy claim.

Objective

The following report corrects the statistical analysis omission in Mr. Böckler's NephroFlow performance study so as to answer the question: "Based on this data, is the NephroFlow's access flow measurement a safe and effective substitute for a Transonic HD03 access flow measurement?" And, "If there are differences, do the differences have implications for patient care?"

Vascular Access Flow: Are NephroFlow and Transonic

Statistical Analysis

From the Böckler comparison graph (ibid, Abb.5), Transonic identified 75 out of the 79 access flow (Qa) measurements. (Four others seem to have the same values and could not be recovered from the graph; if these omitted points are normal-distributed within the set, their omission should not significantly impact a statistical analysis.) These 75 data points were used for the following statistical analysis: #1 Critchley and Critchley criterion³ and #2 Accuracy Specification.

We calculated percent error (PE) for the 75 observations. NephroFlow access flow reading (QaNF) against its reference Transonic reading (QaHD03).

- PE defines the 95.4% confidence limits: about 19 of 20 QaNF would fall between these limits if their distribution were Gaussian ("normal").
- $PE = 2 * SD / \text{Mean}$, where SD is the standard deviation of the (QaNF - QaHD03) data sets.
- Mean is an average of all (QaNF+QaHD03)/2 data points.
- Bias is defined as the average of the (QaHD03 - QaNF) data points, the average difference between the two methods.

First Criterion: Critchley and Critchley Analysis³ Using the Bland-Altman Test⁴

This criterion analyzes the percent error PE, graphically presented in a (linear) Bland-Altman plot (Fig.1). For the 75 data points, $PE = 2 * 210 / 1033 * 100\% = 40.6\%$. Critchley and Critchley teach that two methods that both claim the same absolute accuracy (AbAc) will be interchangeable if PE is equal or less than $\sqrt{2} * \text{AbAc}\%$ (if their scatter is Gaussian). Both HD03⁵ and NephroFlow⁶ specify $\pm 15\%$ absolute accuracy for the larger part of their measurement range, the Critchley-Critchley margin for agreement between the two Qa measurement devices is therefore $PE \leq \sqrt{2} * 15\% = 22\%$.

The Critchley-Critchley criterion leaves no room for doubt. Access flow reported by NephroFlow is not interchangeable with the HD03 access flow measurement because the observed percent error of 40.6% is nearly two times larger than the required 22%.

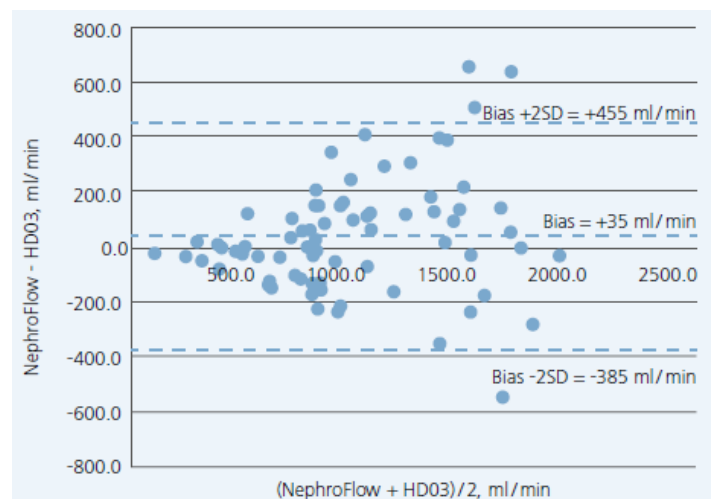


Fig.1 Bland Altman Plot of NephroFlow vs. HD03: Flow based on Abb.5 [1] (includes 75 points out of 79). Percent Error is 40.6%; per Critchley and Critchley criterion this indicates that NephroFlow may not be used to implement Guidelines derived with the Transonic HD Monitors.

Second Criterion: Accuracy Specifications

Transonic and Nipro D.Med publish the same measurement accuracy specification for access flow: that its Qa reading represents true flow within the larger of $\pm 15\%$ and $+100 \text{ mL/min}$ ^{5,6} (i.e., $\pm 100 \text{ mL/min}$ for $Qa < 667 \text{ mL/min}$, $\pm 15\%$ for $Qa \geq 667 \text{ mL/min}$). Thirty-one of the 75 NephroFlow readings in the Böckler data set (41%) are more than 100 ml/min and 15% off their reference HD03 reading. This produced a large data scatter for the reported NephroFlow vs HD03 Flow (Fig. 2a). For visual indication of the amount of measurement error introduced by the NephroFlow, we plotted in Fig.2b the same HD03 data points on the horizontal axis, and added to each data point its absolute accuracy tolerance scatter (calculated as random Gaussian data noise) of $\pm 15\%$, $\pm 100 \text{ mL/min}$. Fig. 2b presents how a Transonic HD Monitor represents true Qa flow. Fig. 2a illustrates the amount of data scatter that is added by the NephroFlow implementation.

Visual comparison of these two graphs illustrates that the Böckler data could not possibly be equivalent to Transonic HD03 data within ($\pm 15\%$, $\pm 100 \text{ mL/min}$): the scatter of its data points is about 2x greater.

HD03 Hemodialysis Monitor Measurements Interchangeable?

Practical Implications

While the analysis reveals large statistical differences between data sets, the clinical user must deal with individual measurements. The large variability of the NephroFlow may lead to mistakes in diagnosis, both false positives where NephroFlow could lead to studies and treatments in patients who may not need them, and false negatives where NephroFlow would not flag conditions in patients who are indicated for further studies and treatments. Either instance is suboptimal treatment and harm to the patient.

As an example, if the NephroFlow were to be used to implement KDOQI/European guideline "An access flow in AV grafts < 600 mL/min is an indicator for pre-emptive intervention" then in Fig.2a the three points marked a-b-c would be false positives (NephroFlow reports flows around 570-580 mL/min; HD03 reports flows in the 710-740 range).

The same Guideline recommends screening for a drop in access flow >20% within one month (grafts) or three months (fistulae). For the points d and e in Fig. 2a, the HD03 reported flows around 870 mL/min. NephroFlow could read during one screening: 1290 mL/min (point d), and 43% less at a next screening (730 mL/min, point e) to trigger a false positive indicator for pre-emptive screening. In clinics where "access flow > 2 L/min" is used as an indicator for access banding or other intervention, point f would be a false positive (NephroFlow > 2L/min, HD03 ~ 1.45 L/min); point g would be a false negative (NephroFlow ~ 1.45 L/min, HD03 > 2 L/min).

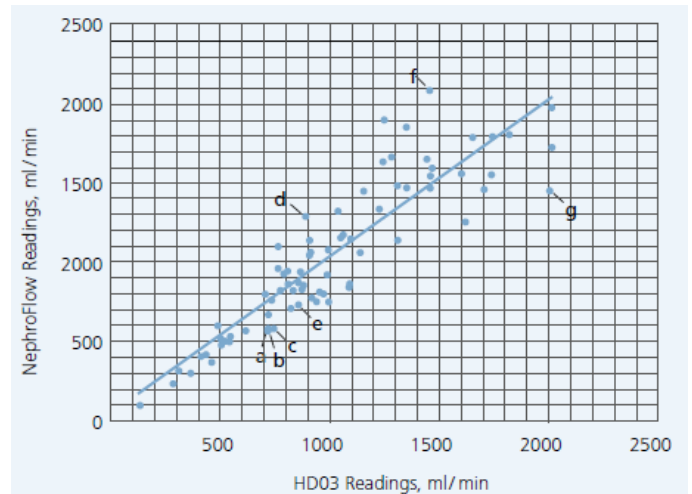


Fig. 2a: Böckler data, reprinted as NephroFlow readings against their reference HD03 measurements.

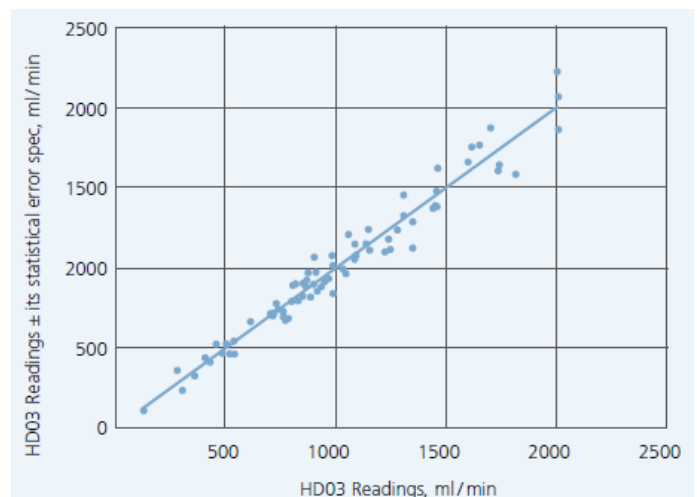


Fig.2b. The same Böckler HD03 readings, "seeded" with the HD03 specification tolerance (normal Gaussian distribution) of $\pm 15\%$, ± 100 mL/min.

Statistical Summary

1. Bland Altman analysis of the Böckler data set yields a Standard Error of 41%, nearly twice the medical industry margin of 22% (Critchley-Critchley).
2. More than one third of the data points in the Böckler data set show differences between NephroFlow and HD03 readings that exceed both technologies' accuracy specifications.

Conclusion

Access flow measured by NephroFlow and access flow measured by the Transonic HD03 are not interchangeable. Using the NephroFlow to execute Transonic-derived patient management guidelines may lead to poor clinical decisions that could affect patient outcomes.



The Transonic Hemodialysis Monitor measures blood flow in a vascular access to identify stenoses and to extend the life of the vascular access.

References

- 1 Krivitski N, "Theory and validation of access flow measurement by dilution technique during hemodialysis," *Kidn Int.* 1995; 48(1): 244-250.
- 2 Böckler H, D.Med Consulting AG, "Apparatives Shunt Monitoring, Teil 2," *Spectr Dial Apher* 2016; 06(2): 26-29 (in German)
- 3 Critchley LA, Critchley JA, "A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques," *J Clin Monit Comput.* 1999; 15(2): 85-91.
- 4 Bland JM, Altman DG, "Statistical methods for assessing agreement between two methods of clinical measurement," *Lancet* 1986; 1: 307-310.
- 5 Operator's Manual - Transonic HD03 Hemodialysis Flow-QC Monitor, p 7.
- 6 Operating Instruction D.Med NephroFlow™ Clinical Manual-en Version 3.0, p 33.