Received: 13 June 2022 | Revised: 25 August 2022 | Accepted: 13 September 2022

DOI: 10.1111/pan.14563

Pediatric Anesthesia WILEY

SHORT REPORT

Reference values in healthy children using the Quantra Hemostasis Analyzer, a novel point of care viscoelastic testing device

Sundeep Tumber[1] | Casey Stondell[1] | Machelle Wilson[2] | Nuen Tsang Yang[2] | Sampaguita Tafoya[1]

[1]Department of Anesthesiology, Shriners Children's, Northern California, Sacramento, California, USA

[2]Department of Public Health Sciences, School of Medicine, University of California, Davis, Sacramento, California, USA

Correspondence
Sundeep Tumber, Shriners Children's, Northern California, Department of Anesthesiology, 2425 Stockton Blvd., Sacramento, CA 95817, USA.
Email: stumber@shrinenet.org

Several recently developed transfusion guidelines recommend the use of viscoelastic testing (VET) to help guide blood component therapy for pediatric patients undergoing major surgery.[1] In contrast to traditional lab testing, VET measures each stage of coagulation including clot initiation, strength, and lysis. VET can detect specific defects in coagulation such as hypofibrinogenemia, hyperfibrinolysis, and platelet function.[2] Recently, Hass and Faraoni summarized the current pediatric literature and reference range results of traditional VET devices. The authors concluded that adult reference ranges for VET could be applied over the age of 1 year.[1]

The two most common VET modalities used in the USA, rotational thromboelastometry (ROTEM® Delta, TEM International GmbH) and thromboelastography (TEG® 5000, Haemonetics Corporation), employ similar technologies, consisting of an oscillating pin suspended in a cup of blood. Clotting exerts increasing resistance on the pin, and the contributors to clot formation are thus determined.[2] The Quantra Hemostasis Analyzer (HemoSonics LLC) is a newer, automated, cartridge-based point of care (POC) VET device based on sonic estimation of elasticity via resonance (SEER) technology, allowing direct measurement of the viscoelastic properties of clot formation by utilizing ultrasound technology. Blood is placed into a 2.7 ml standard citrated laboratory tube and inserted into a QPlus® cartridge. Ultrasound waves pulse into the sample to induce resonance, causing the sample to oscillate. As the blood coagulates, its stiffness and frequency of oscillation increase. Clot time and clot stiffness values are measured from the evolving shear modulus (the resistance of the sample to shear forces).[3] This technology provides novel diagnostic data that may guide component transfusion therapy. The QPlus Cartridge reports four directly measured parameters: clot time (CT), heparinase clot time (CTH), clot stiffness (CS), and fibrinogen contribution to clot stiffness (FCS). Platelet contribution to clot stiffness (PCS) is calculated and reported as the difference between CS and FCS.

There are currently no published pediatric reference ranges for the Quantra. In this report, we present the results of VET using the Quantra device in 50 healthy pediatric subjects undergoing elective surgery. This sample size was guided by the Clinical Laboratory Standards Institute EP28-A3c for reference range verification.[4]

After IRB approval (NCA2106), consent was obtained for 50 healthy ASA 1 and 2 patients aged 2–17 years undergoing elective noncardiac surgical procedures including orthopedic, urologic, plastic, and general surgery. Exclusion criteria included known bleeding disorders, sepsis, or medications that could affect coagulation. Blood samples were collected during intravenous catheter placement, and specimens were analyzed using the Quantra system. Data for 50 patients (30 male and 20 female) were collected. Median age was 12 years (IQR 6 years), median height was 155 cm (IQR 35 cm), and median weight was 50.1 kg (IQR 34.8 kg).

Summary statistics were reported as medians and interquartile ranges. Outliers with p-value less than 0.05 were excluded using the Dixon's test. The reference ranges were determined between the 2.5 and 97.5 percentiles using the Excel® quantile functions. Additionally, 90% confidence intervals for the lower and upper bounds of the

Section Editor: Susan Goobie

TABLE 1 Quantra hemostasis analyzer pediatric reference range results and reported adult reference ranges

Parameter	Units	Pediatric lower bound (90% CI)	Pediatric Upper bound (90% CI)	Adult lower bound[a] (95% CI)[b]	Adult upper bound[a] (95% CI)[b]
Clot time (CT)[c]	Sec	105 (92, 117)	176.1 (169, 185)	104 (99, 115)	166 (158, 172)
Heparinase clot time (CTH)[c]	Sec	106 (89, 110.9)	165.8 (154, 170)	103 (92, 114)	153 (145, 160)
Clot stiffness (CS)[c]	hPa	13.8 (13.8, 15.1)	35.1 (30.1, 45.3)	13.0 (11.6, 14.6)	33.2 (29.7, 35.3)
Platelet contribution to clot stiffness (PCS)[d]	hPa	12.8 (12.5, 14.1)	32 (26.3, 39.9)	11.9 (10.7, 13.6)	29.8 (27.1, 31.0)
Fibrinogen contribution to clot stiffness (FCS)[c]	hPa	0.9 (0.8, 1.0)	3.9 (3.1, 4.0)	1.0 (0.9, 1.2)	3.7 (3.4, 3.8)

Abbreviations: CI, confidence interval; hPa, hectopascal; sec, seconds.
[a]Adult Reference ranges from QPlus cartridge instructions for use.
[b]HemoSonics, LLC.
[c]Directly measured parameter.
[d]Reported parameter, calculated as the difference between CS and FCS.

reference ranges were generated via a nonparametric bootstrap approach using the *sample*, *quantile*, and *sort* functions in R version 3.6.1.

Results are shown in Table 1 and were obtained in 11.3 min on average (SD 1.8). Only FCS had one outlier of 5.4 hPa ($p = .007$). Our results were similar to healthy adult reference ranges, with the confidence intervals around the upper and lower bounds of the pediatric ranges overlapping with the adult ranges.

Advantages of the Quantra are that it utilizes a standard blue-top lab tube and provides POC results in less than 15 min. By contrast, TEG and ROTEM typically require transport to a central location, trained technicians to pipette and process samples, and up to 30–45 min for complete results.[2] One potential limitation of the Quantra is that it requires 2.7 ml of blood per sample, as compared to <1.0 ml for TEG 5000 and ROTEM Delta.

The Quantra has been validated against conventional coagulation testing as well as ROTEM delta and TEG 5000.[3,5] The advantages of the Quantra are its rapid turnaround time and ease of use, which facilitates POC testing. This may allow for real-time goal-directed blood product transfusions in patients experiencing rapid blood loss; more research is needed.

CONFLICT OF INTEREST

The authors report no relevant conflicts of interest for this manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Sundeep Tumber https://orcid.org/0000-0002-7925-6468
Casey Stondell https://orcid.org/0000-0002-2960-9819
Sampaguita Tafoya https://orcid.org/0000-0002-6672-6109

REFERENCES

1. Haas T, Faraoni D. Viscoelastic testing in pediatric patients. *Transfusion*. 2020;60(Suppl 6):S75-S85.
2. Carll T, Wool GD. Basic principles of viscoelastic testing. *Transfusion*. 2020 Oct;60(Suppl 6):S1-S9. doi:10.1111/trf.16071
3. Reynolds PS, Middleton P, McCarthy H, Spiess BD. A comparison of a new ultrasound-based whole blood viscoelastic test (Seer sonorheometry) versus thromboelastography in cardiac surgery. *Anesth Analg*. 2016;123(6):1400-1407.
4. Clinical Laboratory Standards Institute EP28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline–3rd Edition.
5. Groves DS, Welsby IJ, Naik BI, et al. Multicenter evaluation of the Quantra QPlus system in adult patients undergoing major surgical procedures. *Anesthesia & Analgesia*. 2020;130(4):899-909.

How to cite this article: Tumber S, Stondell C, Wilson M, Yang NT, Tafoya S. Reference values in healthy children using the Quantra Hemostasis Analyzer, a novel point of care viscoelastic testing device. *Pediatr Anesth*. 2022;32:1370-1371. doi: 10.1111/pan.14563