Journal of Clinical Virology 91 (2017) 5–11

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

The New Aptima HCV Quant Dx Real-time TMA Assay Accurately Quantifies Hepatitis C Virus Genotype 1-6 RNA

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ARTICLE INFO

Article history:
Received 22 September 2016
Received in revised form 6 March 2017
Accepted 27 March 2017

Keywords:
HCV RNA quantification
TMA
Direct-acting antivirals
Monitoring of viral responses

ABSTRACT

Background: Sensitive and accurate hepatitis C virus (HCV) RNA detection and quantification is essential for the management of chronic hepatitis C therapy. Currently available platforms and assays are usually batched and require at least 5 hours of work to complete the analyses.
Objectives and study design: The aim of this study was to evaluate the ability of the newly developed Aptima HCV Quant Dx assay that eliminates the need for batch processing and automates all aspects of nucleic acid testing in a single step, to accurately detect and quantify HCV RNA in a large series of patients infected with different HCV genotypes.
Results: The limit of detection was estimated to be 2.3 IU/mL. The specificity of the assay was 98.6% (95% confidence interval: 96.1%-99.5%). Intra-assay and inter-assay coefficients of variation ranged from 0.09% to 5.61%, and 1.05% to 3.65%, respectively. The study of serum specimens from patients infected with HCV genotypes 1 to 6 showed a satisfactory relationship between HCV RNA levels measured by the Aptima HCV Quant Dx assay, and both real-time PCR comparators (Abbott RealTime HCV and Cobas AmpliPrep/Cobas TaqMan HCV Test, version 2.0, assays).
Conclusions: the new Aptima HCV Quant Dx assay is rapid, sensitive, reasonably specific and reproducible and accurately quantifies HCV RNA in serum samples from patients with chronic HCV infection, including patients on antiviral treatment. The Aptima HCV Quant Dx assay can thus be confidently used to detect and quantify HCV RNA in both clinical trials with new anti-HCV drugs and clinical practice in Europe and the US.

1. BACKGROUND

Sensitive nucleic acid amplification technologies (NAATs) are recommended for HCV RNA detection and quantification by international Clinical Practice Guidelines [1–3], and now widely used in clinical virology laboratories. These assays are fully or partly automated. With a broad range of linear quantification, a limit of detection (LOD) of the order of 10 to 15 international units per milliliter (IU/mL), and an identical LOD and lower limit of quantification (LLOQ) for the most recent assays, these techniques are well suited to the clinical needs [4]. Among them, Cobas AmpliPrep/Cobas TaqMan HCV Test, version 2.0 (CAP/CTM HCV v2.0, Roche Molecular Systems, Pleasanton, CA) and Abbott RealTime HCV (Abbott Molecular, Des Plaines, IL) are the most widely used assays. They have satisfactory performance for HCV RNA detection and quantification in clinical practice [5–7]. Currently available platforms and assays are usually batched, and many laboratories struggle to provide results within a one-full-day window. The Aptima HCV Quant Dx assay (Hologic Inc., San Diego, CA) is a transcription-mediated amplification (TMA)-based assay making use of the fully automated Panther system that eliminates the need for batch processing and automates all aspects of nucleic acid testing on a single step, shortening the time needed to obtain results. Approximately 2.5 hours are required to obtain the first five results, then 5 more results are obtained every 5 minutes.

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http://dx.doi.org/10.1016/j.jcv.2017.03.020
1386-6532/

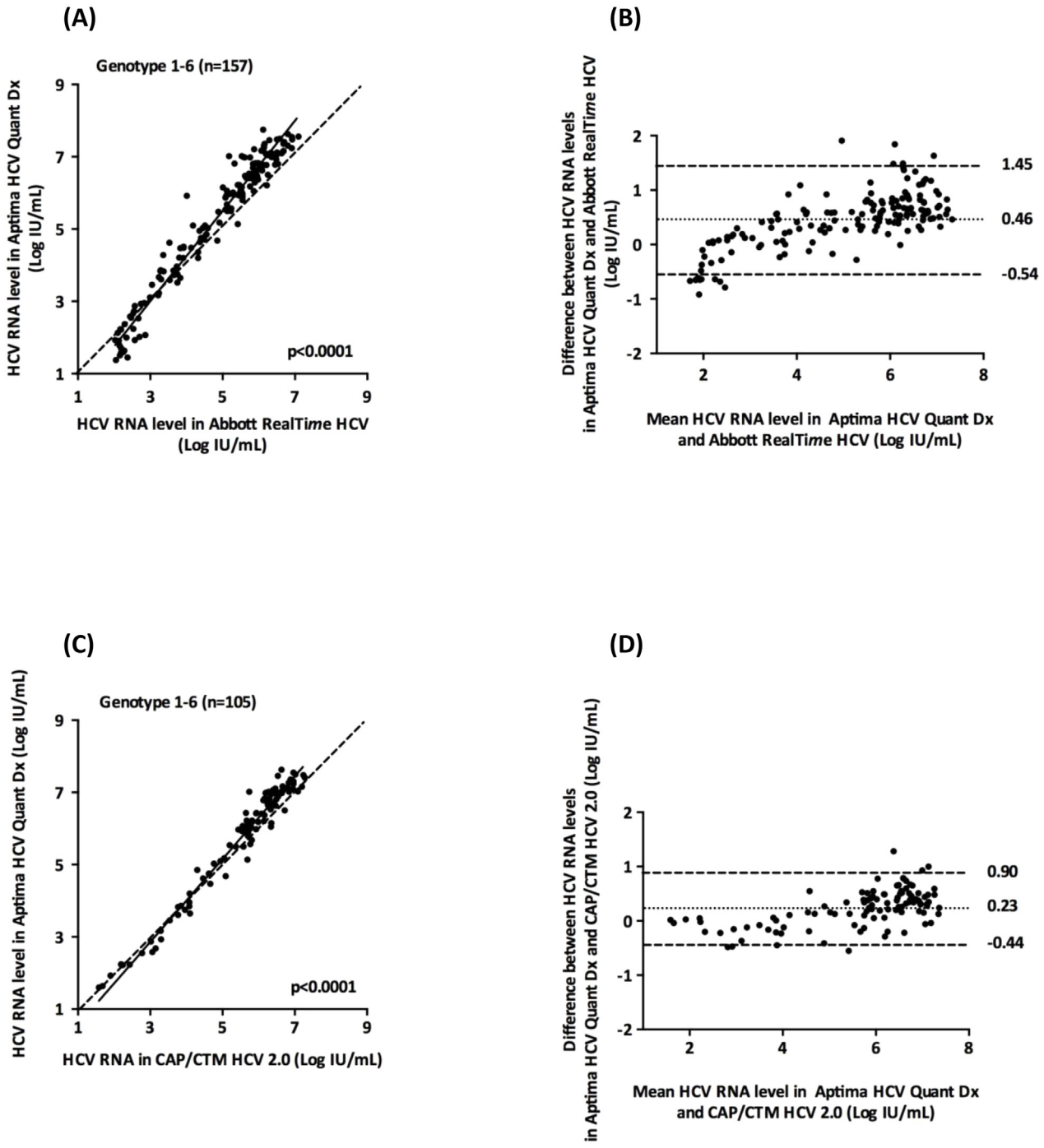

Fig. 1. Deming correlation and Bland-Altman plot analysis of HCV RNA levels measured by Aptima HCV Quant Dx in 162 clinical specimens (Group B) containing HCV genotype 1 (n = 51), 2 (n = 22), 3 (n = 44), 4 (n = 37), 5a (n = 2), 6 (n = 4), or an indeterminate genotype (n = 2). (A) Deming regression of HCV RNA levels measured by Aptima HCV Quant Dx and Abbott RealTime HCV, respectively. (B) Bland-Altman plot analysis of Aptima HCV Quant Dx *versus* Abbott RealTime HCV. (C) Deming regression of HCV RNA levels measured by Aptima HCV Quant Dx versus CAP/CTM HCV 2.0. (D) Bland-Altman plot analysis of Aptima HCV Quant Dx *versus* CAP/CTM HCV 2.0. In the Bland-Altman graph, the dotted and dashed lines represent the mean difference and the ±1.96 standard deviation, respectively.

2. OBJECTIVE

The aim of the present study was to evaluate the ability of the newly developed Aptima HCV Quant Dx assay to accurately detect and quantify HCV RNA in a large series of patients infected with different HCV genotypes.

3. STUDY DESIGN

3.1. Standards

A standard panel (AcroMetrix® HCV-S Panel; Thermo Fisher Scientific, Fremont, CA) was used. Each panel member contains a predetermined level of HCV RNA, calibrated against the WHO International Standard, thus reported in IU/mL. The seven panel