Use of viability PCR results in earlier de-isolation of ICU patients in the CoLaIC study

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Introduction: Patients admitted to the ICU with COVID-19 are placed in isolation until two subsequent negative SARS-CoV-2 PCRs. The question is if the detected viral RNA represents intact virus or compromised viral particles. To distinguish intact infectious virus from incomplete virus or RNA remnants, a viability-PCR method can be used. We hypothesize that the time to a negative PCR would be shorter using the viability-PCR compared to conventional SARS-CoV-2 PCR.

Materials and Methods: Patients admitted to the ICU in two hospitals in Limburg were prospectively included, and respiratory samples were collected three times per week. Samples were aliquoted for viability-PCR and regular SARS-CoV-2 PCR. The vial for viability-PCR was split and treated with propidium monoazide (PMA) for elimination of incomplete virus or untreated. The PMA-untreated vial roughly corresponds with the conventional SARS-CoV-2 PCR used in routine diagnostics.

Using time to a negative PCR test as the outcome, the Paired Prentice-Wilcoxon-test (PPW-test) was used to test for a significant difference in time to negative between viability and conventional SARS-CoV-2 PCR. The PPW test was performed using Ct 35 as the cut-off above and a test result was considered negative. A mean time difference between viability and regular PCR was estimated, assuming a negative binomial distribution.

Results: 102 patients admitted to the ICU were included for statistical analysis. Time to negative PCR test results differed significantly between PMA untreated and PMA treated samples (PPW-test p-value = 0.04)(figure 1). On average, the first negative viability PCR test result occurred 2.39 days (standard error 0.92 days) before the first negative PMA-untreated PCR test result.

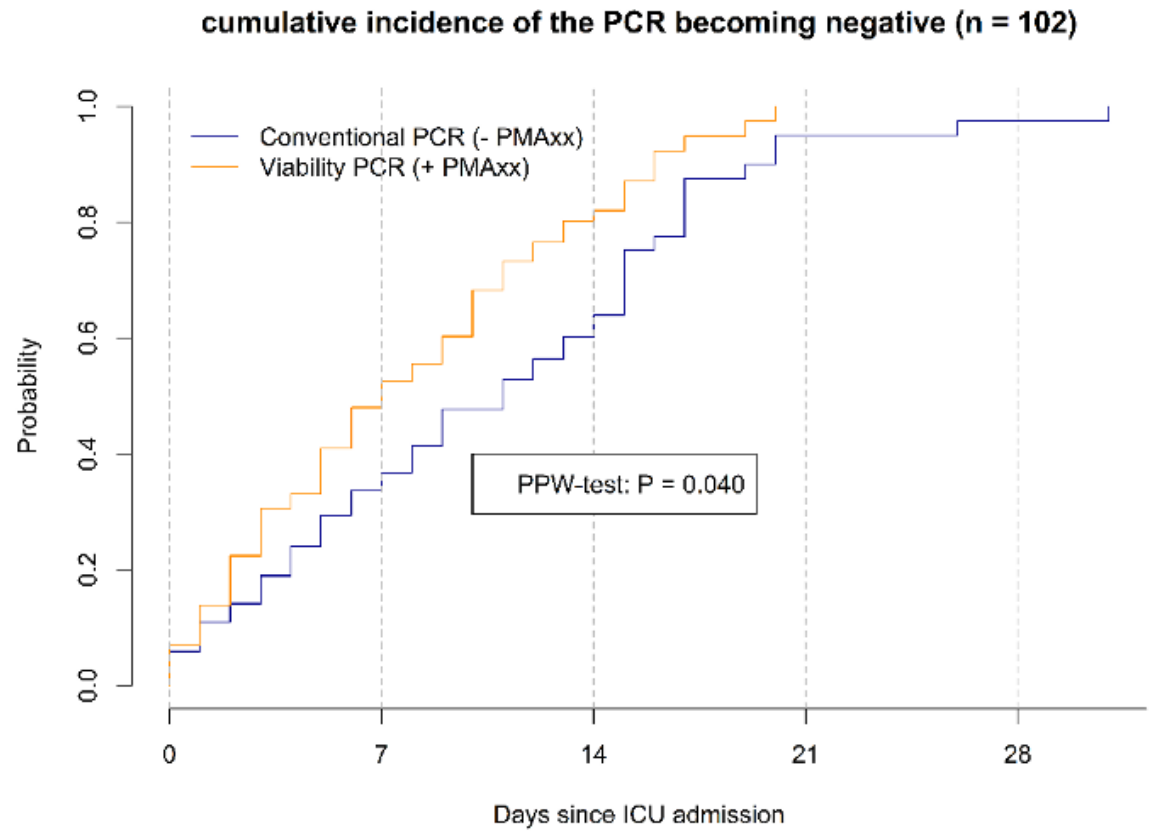

Figure 1: cumulative incidence.
Cumulative incidence plot of the normal PCR and viability PCR becoming negative. The Y axis shows the probability of becoming negative and the X axis shows the days since ICU admission. The Paired Prentice-Wilcoxon-test (PPW-test) showed the difference between the PCR's is statistically significant.

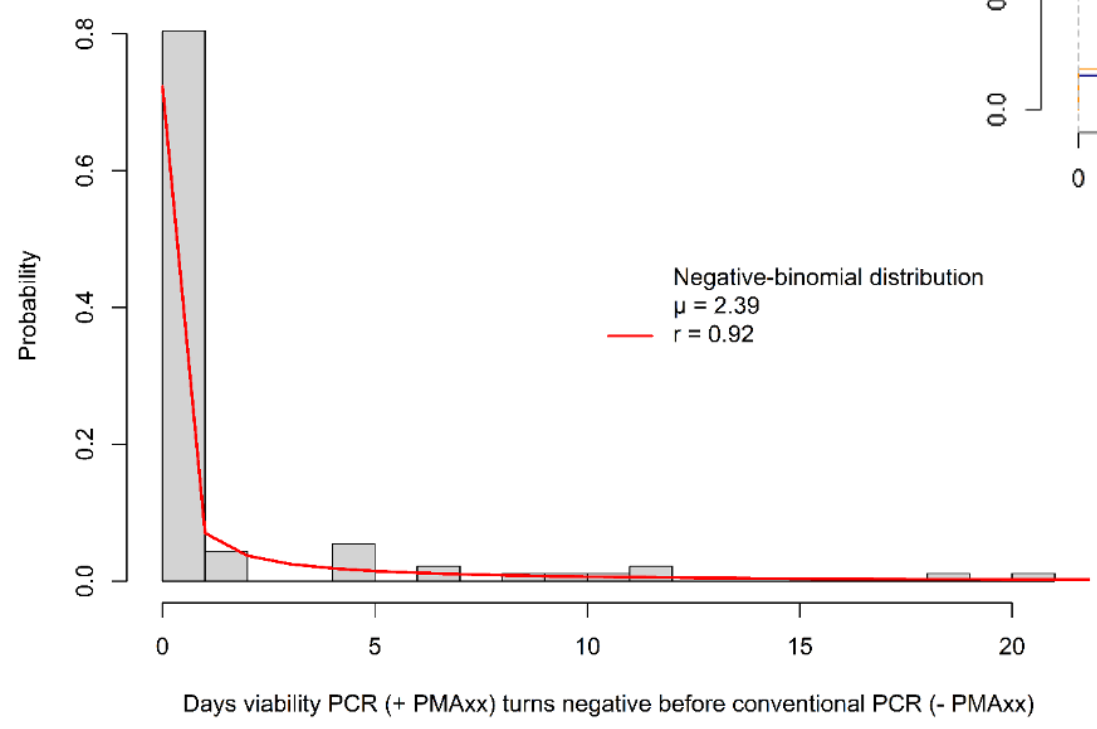

Figure 2: Distribution of the time difference between the viability (+PMAxx) and conventional (-PMAxx) PCR becoming negative.
This figure shows the time difference distribution between the test becoming negative. Population density is shown on the Y axis, and the x-axis, the difference in days between the conventional PCR and viability PCR negativity. If they both became negative on the same day this would be zero and if the viability PCR was negative first a positive time difference is shown. No negative differences indicated that the conventional PCR didn't become negative before the viability within this study. A negative-binomial distribution (red line) was fitted on the data to assess the average time difference (2.39 days (95%CI 0.59 - 4.19) earlier)

Conclusion: Viability PCR for SARS-CoV-2 could provide a more accurate indication of the presence of intact virus and therefore infectivity, potentially enabling earlier de-isolation of ICU patients.

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