SERUM AND URINE NUCLEIC ACID SCREENING TESTS FOR POLYOMAVIRUS-ASSOCIATED NEPHROPATHY IN KIDNEY AND KIDNEY-PANCREAS TRANSPLANT RECIPIENTS: DIAGNOSTIC TEST ACCURACY REVIEW

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The authors have no conflicts of interest to declare.

Please note there have been some changes since the abstract submission.

BACKGROUND AND OBJECTIVE

- BK polyomavirus-associated nephropathy (BKPyVAN)
  - affects a transplanted kidney,
  - leading to an initial injury characterised by cytopathic damage, inflammation, and fibrosis.
  - may cause permanent loss of graft function and premature graft loss.

- Early detection allows clinicians to intervene by timely reduction in immunosuppression to reduce adverse graft outcomes.
- Quantitative nucleic acid testing (QNAT) for the detection of BKPyV DNA in blood and urine is increasingly used as a screening test

- Our objective is to determine the diagnostic test accuracy of QNAT tests for diagnosis of BKPyVAN.

METHODS AND RESULTS

Methods

- We performed a systematic review to determine the diagnostic test accuracy of QNAT tests for the diagnosis of BKPyVAN.
- We searched MEDLINE, EMBASE, Cochrane and other databases until June 2023 and included cohort studies assessing the diagnostic accuracy of blood or urine BKPyV QNAT for the diagnosis of BKPyVAN, as verified by the reference standard (histopathology).
- We assessed the methodological quality by using QUADAS-2 assessment criteria.
- We used the bivariate random-effects model to obtain the summary estimates.
- We explored possible sources of heterogeneity by adding covariates to meta-regression models.

Results

- We included 31 relevant studies with a total of 6559 participants in this review including 18 studies (3434 participants) reporting a common viral load threshold of 10,000 copies/ml in blood.

RESULTS CONTINUED:

Blood QNAT for BKPyVAN:

- The summary estimates of the test of blood BKPyV QNAT test at a threshold of 10,000 copies/mL
  - sensitivity 0.86 (95% CI 0.78 to 0.93) and specificity 0.95 (95% CI 0.91 to 0.97).
- A limited number of studies were available to analyse the summary estimates for individual viral load thresholds other than 10,000 copies/ml. Indirect comparison of thresholds were uncertain, primarily due to a limited number of studies with wide confidence intervals contributed to the analysis.
- The multiple cutoffs model showed that the optimal cut-off was around 2000 copies/ml
  - sensitivity of 0.89 (95% CI 0.66- 0.97) and specificity of 0.88 (95% CI 0.80- 0.93).
  - However, the majority of included studies were retrospective, and not all participants underwent the reference standard resulting in a high risk of selection and verification bias.

Urine QNAT for for BKPyVAN:

- There was insufficient data to thoroughly investigate both accuracy and thresholds of urine BKPyV QNAT resulting in an imprecise estimation of its accuracy based on the available evidence

CONCLUSIONS

- There is insufficient evidence to suggest the use of urine BKPyV QNAT as the primary screening tool for BKPyVAN.

- The summary estimates of the test of blood BKPyV QNAT test at a threshold of 10,000 copies/mL for BKPyVAN
  - sensitivity 0.86 (95% CI 0.78 to 0.93) and specificity 0.95 (95% CI 0.91 to 0.97).
- The multiple cutoffs model showed that the optimal cut-off was around 2000 copies/ml
  - sensitivity of 0.89 (95% CI 0.66- 0.97) and specificity of 0.88 (95% CI 0.80- 0.93).
- While 10,000 copies/ml is the most commonly used cut-off, with high performance supporting the current recommendations, it is important to interpret the results cautiously due to the inherent imprecision of low-certainty evidence.