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Enhancing Pediatric Kidney Transplant Rejection Detection By Integrating The Absolute Copy Number Per ml Of Donor-derived Cellfree Dna To The Donor Percentage Fraction.

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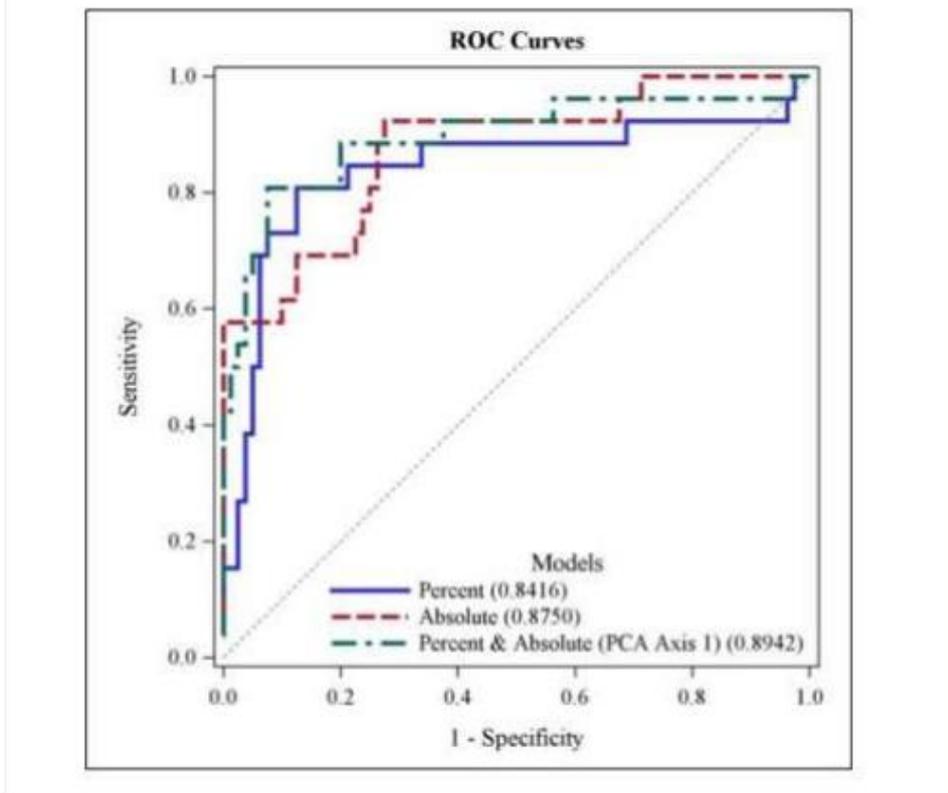
Objectives : Donor-derived cell-free DNA (dd-cfDNA) in blood monitors kidney allograft health. % dd-cfDNA, donor DNA as a percentage of total cfDNA, faces variability due to recipient cfDNA changes. To address this, quantifying dd-cfDNA in genomic copies per ml was explored. We assessed the predictive power of % dd-cfDNA, genomic copies, and their combination for transplant rejection in pediatric patients.

Methods : In this retrospective single-center observational study, we studied 55 patients (M: F 33:22) who had concurrent 106 dd-cfDNA levels along with kidney biopsies within the three years post-transplant. We included both surveillance biopsies (3, 6 and 12 months post-transplant) and diagnostic biopsies. We quantified dd-cfDNA in plasma as a % fraction of the total cell-free DNA and absolute dd-cfDNA (copies/ml) by next generation sequencing using a targeted, multiplex PCR-based method for the analysis of single nucleotide polymorphisms (AlloSure, CareDx, Brisbane, CA). Treating each sample as independent, we divided the 107 biopsy samples with concurrent dd-cfDNA levels into two groups (no evidence of rejection vs any rejection including subclinical rejection) and analyzed the data.

Results : In patients (n = 26 samples) with biopsy-proven rejection, median dd-cfDNA (cp/ml) was 6 fold higher and median % dd-cfDNA 4-fold higher (90 cp/ml; 0.93%, respectively) than medians in stable phase patients (n = 80 samples) without rejection (15 cp/ml; 0.22%). The AUC of% dd-cfDNA alone to identify rejection was 0.84, the absolute quantification of dd-cfDNA alone was 0.87 and combined AUC improved to 0.89. At the cut off values of 1% and 78 copies/ml the diagnostic performance is summarized in table.

Conclusions : In this retrospective biopsy-matched, dd-cfDNA study in pediatric kidney transplant patients the combination of dd-cfDNA absolute copy number and percentage was more powerful than either dd-cfDNA percent fraction or absolute quantity alone.

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Diagnostic accuracy of donor-derived cellfree DNA levels for detecting biopsy-proven acute rejection

	Sensitivity	Specificity	PPV	NPV
% donorderived cell free DNA	0.77	0.83	0.38	0.96
absolute donor derived cell free DNA9Copies/ml)	0.58	0.98	0.88	0.88
Combination	0.31	1.00	1.00	0.82