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The Future of Tacrolimus Dosing: Harnessing the Potential of CURATE.AI for Tacrolimus Dose Optimisation- Retrospective Data Analysis

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Introduction: Living donor liver transplantation (LDLT) has become a gold standard treatment in paediatric end stage liver disease. Tacrolimus forms the cornerstone of immunosuppression after paediatric LDLT. Standard-of-care for tacrolimus dose titration is conventionally based on physician-guided drug dosing. This, however, leads to frequent deviations from target trough levels due to inter- and intra-patient variability, particularly during the critical early post-operative phase. Tacrolimus has a narrow therapeutic index and under or overexposure leads to clinically significant adverse effects. We explored the applicability of CURATE.AI, a small data, clinically validated artificial intelligence-derived platform, for guiding tacrolimus dosing towards achieving desired therapeutic levels.

Methods: This is a retrospective study of 16 paediatric LDLT recipients (13 males, median age 2 years) at the National University Hospital Singapore from 2011-2018. Each patients' clinical data including tacrolimus dose and corresponding tacrolimus trough was used to generate a personalised CURATE.AI response profile that identifies and recommends an optimal dose to achieve the target treatment outcomes. CURATE.AI is both disease mechanism-independent and indication-agnostic and has dynamic ability to evolve with time. CURATE.AI's predictive performance was then evaluated with metrics that assessed both technical performance and clinical relevance.

Results:

CURATE.AI-guided dosing fared better than standard-of-care physician-guided dosing in terms of percentage days within clinically acceptable tacrolimus levels of 6.5-12 ng/ml (54.55% vs 49.08%). With CURATE.AI-guided dosing, patients could potentially achieve therapeutic range earlier (Figure 1A) and better maintain therapeutic range with dynamic dose adjustments (Figure 1B).

Conclusion: CURATE.AI was able to enhance the accuracy of tacrolimus dosing compared to unaided physician-guided decisions. Prospective studies may reveal its full potential as a clinical decision support system to balance tacrolimus dose optimisation with drug-related toxicities.