# BAASIS for Monitoring Therapy Nonadherence in Clinical Transplantation: Are We There Yet?

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Although advances in immunosuppression strategies have markedly improved 1-y transplant survival to above 90%, depending on the organ type, ~40% to 70% of the allografts are still lost by 10 y.[1–5] Long-term allograft survival is often perturbed by ongoing immunological injury that leads to premature scarring and allograft loss. Nonadherence to immunosuppressive therapy is increasingly recognized as a key contributor to ongoing alloimmune injury and shortened allograft survival.[6] Nonadherence is prevalent in as many as 20% of the patients irrespective of the transplanted organ type, and the efforts to abate it are thwarted by our inability to accurately measure and address it from a behavioral perspective.[7,8] Thus, metrics that promote a better understanding of patient behaviors, perceptions, experiences, and responses to treatment posttransplantation could provide better insight into nonadherence and lead to development of newer and effective mitigating strategies.

Although a variety of assessment measures such as patient self-reports, pill counts, prescription refill rates, and collateral reports by care providers have been used to assess nonadherence, their true clinical utility is limited by their subjectivity and the potential for bias. Calcineurin inhibitor (CNI) trough level variability has been used as a surrogate for immunosuppression nonadherence and has been shown to be associated with poor transplant outcomes. However, CNI variability is influenced by drug absorption and genetic factors that affect their metabolism and trough levels. Additionally, the usage of generic versions of CNIs could further impact CNI trough level variability because of drug formulation variability. Although electronic medication monitoring (EMM) with a microdevice (which records each time a pill bottle is opened) is still the most objective method for evaluating nonadherence, its applicability in routine clinical practice is limited by its poor accessibility and feasibility. In this regard, Basel Assessment of Adherence to Immunosuppressive Medication Scale (BAASIS) was developed as a 6-item self-report questionnaire that assesses the 3 quantifiable phases of medication adherence: (1) initiation (patient takes the first dose of a prescribed medication), (2) implementation (the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen), and (3) discontinuation (patient stops taking the prescribed medication against a clinician's advice).[9]

In the current issue, Denhaerynck and colleagues[10] assessed the validity and reliability of BAASIS by conducting a meta-analysis encompassing 26 studies and 12 109 adult transplant recipients. To prove validity, the authors first confirmed concordance of self-reported nonadherence assessed by BAASIS with other adherence measures such as EMM, collateral adherence estimates by both physicians and nurses, as well as other self-report adherence measures. Given the strong concordance between BAASIS self-report and EMM, and the excessive costs associated with EMM usage, BAASIS self-report could be an inexpensive alternative. Although there was a discordance between EMM assessment of drug holidays and BAASIS self-report, drug holidays were extremely rare (0.4%) in this extensive analysis that assessed 14 962 prescribed medication doses. Despite an overall statistically significant association between nonadherence assessment by BAASIS and CNI trough variability, the effect size was modest (odds ratio, 1.013; 95% confidence interval, 1.002-1.023; $P$ = 0.02) and the associations were inconsistent among participating studies. However, CNI trough variability could be influenced by factors not related to therapy adherence. Next, they have established the association between BAASIS and psycho-behavioral constructs known to be associated with nonadherence such as depressive symptomatology and the variables included in the integrative model of behavioral prediction (barriers, self-efficacy, intention, and beliefs). Assessment of pooled data from 3 randomized controlled trials that evaluated the efficacy of tailored behavioral interventions to improve adherence revealed only a statistically nonsignificant trend (odds ratio, 0.7; 95% confidence interval, 0.49-1.01; $P$ = 0.06) for the effect of the intervention on the BAASIS questionnaire responses. Of note, 2 of the 3 randomized controlled trials utilized EMM to assess medication adherence and found no effect of the studied interventions on EMM-based adherence assessment either. The 30% to 60% variability noted in BAASIS responses when assessed longitudinally could be

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due to the variations in adherence levels over time. Finally, the Flesch Reading Score for BAASIS was 70, suggesting easy readability (seventh grade level). Moreover, the BAASIS instrument is translated into 11 languages, allowing for a widespread usage internationally. Taken together, the authors demonstrated good validity and reliability of BAASIS as a self-report instrument to assess medication nonadherence in transplant recipients.

Despite the recognition of clinical and economic burden of therapy nonadherence in transplantation, routine clinical assessment of nonadherence is not implemented because of inconsistent methodologies and lack of objectivity. Thus, achieving effective, sustainable, and evidence-based adherence monitoring in real-world clinical settings is a major, yet attainable goal for the field. Although patient self-report of medication adherence is often considered as a bias-prone method, reliable patient-report instruments such as BAASIS can easily be integrated into clinical practice. The effort by the authors to comprehensively assess validity and reliability of a simple and affordable self-report instrument (BAASIS) by conducting a meta-analysis encompassing a large patient sample size that reflects a variety of clinical settings, a wide range of time-periods of assessment after transplantation (ranging from time 0 to a median of ~109 mo posttransplantation), and patient populations in multiple countries is commendable. Although the authors present compelling arguments to support the validity and reliability of BAASIS, the true clinical utility of this instrument could potentially be further enhanced if it is used in conjunction with other measures of nonadherence. Importantly, lack of data on measurable objective clinical end points such as biopsy proven acute rejection, detection of donor-specific antibody and graft or patient survival limits its true clinical applicability. Confirmation of its clinical predictive ability could potentially take this simple self-report instrument much closer to routine clinical application. Moreover, assessment of its validity and utility in select clinical settings (eg, after an episode of acute rejection, when nonadherence has been shown to be a key modifier variable for clinical outcomes) could allow risk-stratification and simplify recruitment of patients into future clinical trials testing novel behavioral/psychological/pharmacologic approaches aimed at mitigating immunosuppression nonadherence. Nonetheless, the meta-analysis by Denhaerynck and colleagues, which confirms the validity and reliability of BAASIS in a large patient cohort, is a major step forward toward the goal of developing objective and usable nonadherence assessment tools in clinical transplantation.

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