Re: Invasive Urodynamic Investigations in the Management of Women with Refractory Overactive Bladder Symptoms (FUTURE) in the UK: A Multicentre, Superiority, Parallel, Open-label, Randomised Controlled Trial

Abdel-Fattah M, Chapple C, Cooper D, et al

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Experts' summary:
The aim of FUTURE, a UK randomised controlled trial, was to assess the clinical and economic value of urodynamics + comprehensive clinical assessment (CCA) in comparison to CCA only for women with refractory overactive bladder (OAB; $n = 1099$). At 15 mo, participant-reported management success was not superior in the urodynamics + CCA arm. The authors conclude that urodynamics was not cost-effective and that the study will change clinical guidelines, with invasive treatment such as botulinum toxin offered to this patient population in the future on the basis of CCA alone.

Experts' comments:
An explicit part of the original premise of the FUTURE trial was the word "routine" [1]. Only "routine use" of urodynamics was in question at study outset but, mysteriously, the word "routine" is now nowhere to be seen, permitting the sweeping conclusion that in refractory OAB, even selective urodynamics has no value. Since the OAB population is inherently heterogeneous, patient phenotyping to guide individualised management is a well-accepted strategy [2]. Unfortunately, the approach in this study—a return to monolithic thinking and empiricism—runs counter to this.

As in the VALUE and VUSIS-II studies in stress urinary incontinence [3,4], choice of therapy in FUTURE study—for which outcomes were ultimately judged—was made not via urodynamic insights but according to local standard practice, which essentially misses the whole point of urodynamics. How urodynamics was used in this study remains obscure; detection of the presence or absence of detrusor overactivity (a major oversimplification of its role) seems to have been the main purpose. Moreover, we have reason to doubt how well the study population reflects the real world. Defining refractory OAB simply as "failure of two sequential oral drugs" is not aligned with the definition of any scientific society [5]. We also suspect that enrolment may not have been consecutive; the surprisingly low overall success rate for treatment suggests an unusually refractory cohort.

Despite these design shortcomings, we note that urodynamics (1) changed the diagnosis in at least 13% of patients, allowing treatment based on the real cause of their symptoms and (2) led to the same level of patient satisfaction with less invasive management. We doubt that the significantly lower use of botulinum toxin in the urodynamics arm was factored into the cost-effectiveness analysis. With its impressive size and scale, the FUTURE trial could have been a valuable research asset. Unfortunately, rather than moving us forward, the conceptually flawed design and misguided interpretation risk setting us back.

Conflicts of interest: The authors have nothing to disclose.

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Re: Bladder-preserving Trimodality Treatment for High-grade T1 Bladder Cancer: Results from Phase II Protocol NRG Oncology/RTOG 0926

Dahl DM, Rodgers JP, Shipley WU, et al

J Clin Oncol 2024;42:4095–102

Experts' summary:
Dahl et al [1] report results from a prospective trial involving 34 patients who underwent trimodal therapy (TMT) for high-grade (HG) T1 non–muscle-invasive bladder cancer (NMIBC) unresponsive to bacillus Calmette-Guérin (BCG). TMT consisted of maximal transurethral resection, radia-

tion, and systemic chemotherapy. Median follow-up among survivors was 5.1 yr. The primary endpoint of the survival rate free from cystectomy at 3 yr was 88%. The 2-yr recurrence-free survival (RFS) rate was 56%. Other outcomes included 5-yr survival rates of 32% for RFS and 56% for overall survival (OS). Eight patients (24%) died of bladder cancer. There were 18 (49%) serious adverse events (SAEs; grade ≥3) [1].

Experts' comments:

We believe that the results from this study do not support routine use of TMT for NMIBC. We are concerned that the National Cancer Institute clinical trial planning meeting has issued prioritization of further investigation into TMT for high-risk NMIBC given the lack of superior oncologic benefit and the greater toxicities in comparison to intravesical therapies. We have several concerns related to the overly optimistic interpretation of the study results.

First, the choice of cystectomy-free survival as the primary endpoint is problematic. While this is one important outcome, endpoints such as RFS, progression-free survival (PFS), and cancer-specific survival (CSS) are important to first confirm oncologic efficacy and safety.

These oncologic outcomes for TMT are comparable to those for historic salvage intravesical therapies and are likely to be inferior to outcomes for next-generation agents. In a recent large multi-institutional cohort of patients with BCG-unresponsive HG T1 NMIBC who largely received BCG (58%), 5-yr survival rates were 33% for RFS, 75% for CSS, and 61% for OS [2], which are similar to results for TMT. Contemporary salvage therapies are likely to yield superior results. Long-term results for nadofaragene firadenovec and sequential intravesical gemcitabine and docetaxel show 5-yr PFS rates of 97% and 89%, and OS rates of 86% and 66%, respectively [3,4]. Short-term outcomes for cretostimogene and TAR-200 have even more favorable RFS and PFS rates, with almost no patients undergoing cystectomy.

Finally, the toxicity of TMT, with an SAE rate of 49%, is far higher than what is typical and acceptable for most current and future intravesical therapies, for which SAE rates generally range from 0% to 9%.

While we encourage the development of novel effective therapies for NMIBC, we do not believe that TMT is a promising avenue. For another TMT cohort within the ADAPT-Bladder trial, recent results showed a 6-mo complete response rate of only 33% in the durvalumab and external beam radiation therapy combination arm [5]. We recommend against routine off-trial utilization of TMT.

Conflicts of interest: The authors have nothing to disclose.

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Re: Using Deep Learning To Differentiate Among Histology Renal Tumor Types in Computed Tomography Scans

Kan HC, Lin PH et al.

BMC Med Imaging 2025;25:66

Experts' summary:

The paper by Kan et al [1] calls into focus the future of care for renal cell carcinoma (RCC), which is moving towards a synergy between human clinical expertise and artificial intelligence (AI). AI is expected to outperform humans in several areas, including analysis of radiology images, processing of histology reports, preoperative planning using 3D technologies, drug discovery, the creation of synthetic control patients, building predictive models, and improving communication in home-based oncology care. However, humans maintain superiority in domains requiring emotional intelligence and contextual judgment. These include accounting for ethical and social factors, decision-