remains incomplete. Absent mechanistic insight into how BCG induces an antitumor response, the identification of optimal treatment strategies is akin to playing the lottery. While we continue to “buy tickets” (aka clinical trials), the odds of winning are heavily against us. That said, the more of the “winning numbers” we know in advance (elements of BCG’s mechanism of action) the greater the probability of “hitting the jackpot.” Although a meta-analysis of the current literature represents a valuable tool for clinical care, accelerating progress in improving outcomes hinges upon stacking the odds in our favor. Basic science research on BCG’s mechanism of action, as a prelude to asking the correct questions, is the key to improving our probability of success.

Commentary on “Impact of (18) F-fluorodeoxyglucose (FDG)-positron-emission tomography/computed tomography (PET/CT) on management of patients with carcinoma invading bladder muscle.” Mertens LS, Fioole-Bruining A, Vegel E, Vogel WV, van Rhijn BW, Horenblas S, Department of Urology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam Hospital, Amsterdam, The Netherlands.


Abstract

Objective: To evaluate the clinical impact of (18) F-fluorodeoxyglucose (FDG)-positron-emission tomography/computed tomography (PET/CT) scanning, compared with conventional staging with contrast-enhanced CT imaging (CECT).

Patients and methods: The FDG-PET/CT results of 96 consecutive patients with bladder cancer were analysed. Patients included in this study underwent standard CECT imaging of the chest and abdomen/pelvis <4 weeks before FDG-PET/CT. Based on the original imaging reports and recorded tumour stage before and after FDG-PET/CT imaging, the preferred treatment strategies before FDG-PET/CT and after FDG-PET/CT were determined for each patient using an institutional multidisciplinary guideline. One of the following treatment strategies was chosen: (i) local curative treatment; (ii) neoadjuvant/induction chemotherapy; or (iii) palliation. The changes in management decisions before and after FDG-PET/CT were assessed.

Results: The median (range) interval between CECT and FDG-PET/CT was 0 (0–29) days. In 21.9% of the patients, stage on FDG-PET/CT and CECT were different. Upstaging by FDG-PET/CT was more frequent than downstaging (19.8 vs 2.1%). Clinical management changed for 13.5% of patients as a result of FDG-PET/CT upstaging. In eight patients, FDG-PET/CT detected second primary tumours. This led to changes of bladder cancer treatment in another four of 96 patients (4.2%). All the management changes were validated by tissue confirmation of the additional lesions.

Conclusions: FDG-PET/CT provides important additional staging information, which influences the treatment of carcinoma invading bladder muscle in almost 20% of cases. Patient selection for neoadjuvant/induction chemotherapy was improved and futile attempts at curative treatment in patients found to have metastases were avoided.

Commentary

Accurate tumor staging is the cornerstone upon which the optimal and appropriate management of neoplastic disease is based. Although rarely acknowledged as such, the current state of the staging/imaging science is vulgar at best. Yes, we have made tremendous advances in our ability to define local disease extent and identify sites of distant spread. Even so, in the context of the ideal, we have far to go. Consider the fact that to reach the reproducibly detectable size of 1 cm³, a tumor must undergo between 28 and 32 doublings. This represents a number of between 10⁸ and 10⁹ cells! Although it is valid to ask what represents a clinically significant number of cancer cells, few would argue that it is substantially less than 10⁹. Although the article by Mertens et al. provides evidence that, relative to conventional computed tomography (CT), the use of ¹⁸F-fluorodeoxyglucose–positron-emission tomography (PET) in muscle-invasive bladder cancer moves us closer to the goal of detecting ever-lower disease volumes (i.e., fewer tumor cells). The demonstrated clinical relevance of the positron-emission tomography/CT altered staging in directing therapy is illustrative of the central role of staging in disease management. This represents a welcome improvement in the sensitivity and specificity of our available staging tools. However, in the words of Robert Frost there are “miles to go before I (we) sleep.”


Abstract

**Objectives:** To evaluate the safety, tolerability and effectiveness of outpatient (office-based) laser ablation (OLA), with local anaesthetic, for non-muscle-invasive bladder cancer (NMIBC) in an elderly population with and without photodynamic diagnosis (PDD). To compare the cost-effectiveness of OLA of NMIBC with that of inpatient cystodiathermy (IC).

**Patients and methods:** We conducted a prospective cohort study of patients with NMIBC treated with OLA by one consultant surgeon between March 2008 and July 2011. A subgroup of patients had PDD before undergoing OLA. Safety and effectiveness were determined by complications (in the immediate post operative period, at three days and at three months), patient tolerability (visual analogue score) and recurrence rates. The long-term costs and cost-effectiveness of OLA and IC of NMIBC were evaluated using Markov modeling.

**Results:** A total of 74 OLA procedures (44 white-light, 30 PDD) were carried out in 54 patients. The mean (range) patient age was 77 (52-95) years. More than half of the patients had more than three comorbidities. Previous tumour histology ranged from G1pTa to T3. One patient had haematuria for 1 week which settled spontaneously and did not require hospital admission. There were no other complications. The procedure was well tolerated with pain scores of 0-2/10. Additional lesions were found in 21% of patients using PDD that were not found using white light. At 3 months, the percentage of patients who had recurrence after OLA with white light and OLA with PDD were 10.6 and 4.3%, respectively. At 1 year, 65.1% and 46.9% of patients had recurrence. The cost of OLA was found to be much lower than that of IC (£538 vs £1474), even with the addition of PDD (£912 vs £1844). Over the course of a patient's lifetime, OLA was more clinically effective, measured in quality-adjusted life-years (QALY), than IC (0.147 [sd 0.059]) and less costly (£2576.42 [sd £7293.07]). At a cost-effectiveness threshold of £30,000/QALY, as set by the National Institute for Health and Care Excellence, there was an 82% probability that OLA was cost-effective.

**Conclusions:** This is the first study to demonstrate the long-term cost-effectiveness of OLA of NMIBC. The results support the use of OLA for the treatment of NMIBC, especially in the elderly.

Commentary

The term “paradigm shift” is overused and perhaps is a cliché. However, I know of no better term for describing the changes facing health care delivery in the United States. In capitated and/or “at-risk” care delivery systems, the urologist, and everything they do, is slated to change from a revenue stream to a cost center. The implications of this shift are indeed profound. What we do, how and on whom we do it, are poised to change. A focus on value (quality/cost) will mandate a critical review of every aspect of urologic care. This is already taking place in other national health care systems. The article by Wong et al. illustrates the costs savings to the United Kingdom’s National Health Service of using outpatient laser ablation as the primary management strategy for patients with non-muscle-invasive bladder cancer. A recent article from the United States demonstrated a 26-fold reduction in the cost associated with the treatment of hydroceles when aspiration/sclerotherapy was used relative to anesthetic-based surgical repair [1]. These are but the leading edge of a tidal wave of change. A wave that will flip the focus of health care delivery from productivity-based revenue generation to expense reduction through constrained utilization. If previous physician adaptive responses to economic pressures are predictive of future events, I suspect that many current clinical “sacred tenets” will become the new heresy.

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Reference