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Bladder Cancer

Photodynamic Diagnostics and Noninvasive Bladder Cancer: Is It Cost-Effective in Long-Term Application? A Germany-Based Cost Analysis

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Abstract

Objectives: Noninvasive urothelial carcinoma of the bladder (UCB) causes an enormous economic burden to public health systems due to its life-long character and frequent recurrences. While white light (WL) cystoscopy is considered to be the gold standard for transurethral resection of the bladder, photodynamic diagnostic (PDD) has been shown to improve final outcome. Escalating healthcare costs warrant increased effectiveness in treating noninvasive UCB. No data based on assessment of costs have been published to date.

Methods: A series of 301 patients with noninvasive UCB were randomized prospectively to standard WL or PDD transurethral resections of the bladder. Intravesical adjuvant therapy was administered as reflected in the appropriate guidelines. Expenditures of subsequent procedures and PDD-associated costs were assessed.

Results: Median follow-up was 7.1 yr. Disease recurrence was found in 42% and 18% of WL and PDD patients, respectively ($p = 0.0003$). In the WL group 2.0 and in the PDD group 0.8 transurethral resections of the bladder were noted per patient. In the WL group 1.0 and in the PDD group 0.3 recurring UCB occurred per patient, resulting in costs of €1750 per WL patient versus €420 per PDD patient in the follow-up period, respectively. Because a single expenditure of €135 was assessed for PDD, overall costs were significantly lower (by €1195) in PDD patients. As the median follow-up was 7.1 yr, costs saved by PDD per patient per year were €168.

Conclusion: Our data suggest that PDD significantly cut costs related to recurring UCB. Further studies are needed from an economic point of view.

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1. Introduction

An estimated 90,000 urothelial carcinomas of the urinary bladder (UCBs) are expected in the European Union per year [1], and in 80% the cancer is not muscle invasive. Because up to 70% of noninvasive UCB will recur, it has a life-long character and is one of the most costly cancers from diagnosis to death [2,3]. Although data on the economics of UCB are scarce, noninvasive recurrences seem to pose the major cost. Cystectomies have been reported to account for roughly 30% and transurethral resections of the bladder (TURBs) for 40% of the expenditure [4]. Considering the yearly recurrence rate of 35% for noninvasive cases, the economic burden of non-invasive UCB is massive [5].

While white light (WL) cystoscopy is considered the gold standard for the detection of UCB and for the visualization of tumour in TURB, its sensitivity and specificity is not entirely satisfactory. Remnant tumours have been found in up to 43% at secondary resections [6]. To enhance the effectiveness of TURB, fluorescence based photodynamic methods have been evaluated since the mid-1990s. To date 5-aminolaevulinic acid is the best studied [7]. TURB guided by photodynamic diagnostic (PDD) has been reported to enhance tumour detection and reduce recurrences by 20% [8], and tumour-free survival is significantly prolonged [9,10].

Escalating healthcare costs demand evaluation of effectiveness in diagnosing and treating major malignancies. To control expenditures and increase transparency, German legislation has mandated a new remuneration system from 2007 onwards based on diagnosis-related groups. In this system all remunerations are based on the primary diagnosis of the patient and individual disbursement (ie, duration of hospitalization) is no longer relevant [11,12].

PDD has been shown to reduce relapsing UCB while requiring additional expenditures for fluorescent agents and modified blue-light cystoscopies. Although an effective reduction in morbidity and costs by PDD has been suggested by cost estimation [13,14], no detailed economic analysis has been published to date. The aim of the present study was to evaluate whether PDD would reduce costs in comparison to WL based on a previous prospective and randomized study with a primary oncological endpoint [9].

2. Methods

2.1. Study design

Appropriate ethical and written informed consents were obtained. As described previously [9], from May 1997 to August 2000 at the Department of Urology of the University of Regensburg, 301 patients with endoscopic lesions suspicious for UCB were randomized to undergo standard WL- ($n = 150$) or PDD-guided TURB ($n = 151$). Macroscopically tumour-free resection of all lesions was obtained at TURB. To evaluate the residual tumour rate, all patients with noninvasive UCB or CIS underwent secondary WL resection of the former site of surgery 6 wk after initial surgery. Patients with muscle-invasive UCB or nonmalign histopathology were excluded from further investigation. Histopathological evaluation of all specimens was performed according to the 1994 WHO classification and the 1997 TNM system.

2.2. PDD-guided TURB

As described previously [9], patients randomized into the PDD group were given aminolaevulinic acid solution (Medac, Hamburg, Germany) by intravesical instillation. As the light source, a white light bulb with band-pass filter and xenon lamp (Karl Storz GmbH, Tuttlingen, Germany) was used. Fluorescent and otherwise suspicious lesions were resected.

2.3. Adjuvant therapy

Intravesical adjuvant therapy was administered as reflected in appropriate guidelines [15]. Solitary initial pTa G1/2 UCB received no treatment, multifocal pTa/1 G1/2 UCB received mitomycin C. Bacillus Calmette-Guerin was administered in initial pTa/1 G3 UCB, CIS, or recurrences after mitomycin treatment. Recurrent pT1 G3 or CIS underwent cystectomy.

2.4. Follow-up and subsequent costs

Follow-up examinations were performed at 3-mo intervals by WL and cytology. All suspicious findings underwent WL-guided TURB; recurrences were confirmed by histopathology. Follow-up information was collected from all patients until July 2006. Cases requiring subsequent cystectomies due to UCB progressing to muscle-invasive stages were not evaluated further.

Costs for TURBs were calculated according to the ICD and diagnosis-related-groups system. A base rate of €2500 representing most hospitals was assumed; the 2006 cost-weight for UCB undergoing TURB is 0.7, resulting in €1750. Manufacturer information was obtained for calculation of PDD-related costs in the European Union. Aminolaevulinic acid (Medac) is currently distributed at €95 per instillation in Germany. Required modification of standard TURB equipment for PDD use is available at €5000 (range: €2000–7000) in Germany (eg, Olympus Deutschland GmbH, Hamburg, Germany; Karl Storz GmbH, Tuttlingen, Germany; Richard Wolf GmbH, Knittlingen, Germany). To evaluate cystoscope-related costs per PDD, depreciation over 10 yr and 50 uses per year were assumed, resulting in 500 applications and €10 per use. Additional costs for single-use catheterization were €30. Thus, PDD-related cost accounted for €135 (€95 + €10 + €30).

2.5. Statistical analysis

Statistical analyses were performed using SPSS version 12.0 (SPSS, Chicago, IL, USA). Chi-square tests were used to