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Bladder Cancer

Early Versus Deferred Cystectomy for Initial High-Risk pT1G3 Urothelial Carcinoma of the Bladder: Do Risk Factors Define Feasibility of Bladder-Sparing Approach?

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Abstract

Objectives: We compared long-term outcome in patients with initial pT1G3 bladder cancer (BC) treated with early versus deferred cystectomy (CX) for recurrent pT1G3 or muscle-invasive BC after an initial bladder-sparing approach. The aim of this study was to compare survival rates and to analyse the influence of the recognised risk factors multifocality, tumour size, and carcinoma in situ (CIS) in initial transurethral resection of the bladder.

Methods: Between 1995 and 2005, a total of 105 patients were diagnosed with initial pT1G3 BC featuring $\geq$2 risk factors. Forty-five percent had multiple tumours, 73% tumours >3 cm in size, and 46% CIS. All patients were offered early CX. Fifty-one percent of patients opted for early and 49% underwent deferred CX for recurring BC. Risk factors were distributed evenly between the groups.

Results: Upstaging in the CX specimen was found in 30% of cases. No risk factor was related to upstaging. The 10-yr cancer-specific survival rate was 78% in early CX and 51% in deferred CX ($p < 0.01$). No risk factor predicted cancer-related death in early CX. In survival analysis, CIS was related to a lower cancer-specific survival rate in deferred CX ($p < 0.001$).

Conclusions: Early as opposed to deferred CX seems to prolong the cancer-specific survival rate in high-risk pT1G3 BC. Patients with CIS should be considered for early CX owing to reduced cancer-specific survival in case of deferred CX.

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1. Introduction

Urothelial cancer of the bladder (BC) staged as pT1G3 comprises roughly 10% of all non–muscle-invasive tumours [1]. Transurethral resection of the bladder (TURB) is the standard treatment for non–muscle-invasive BC. Despite often being referred to as superficial, pT1G3 BC features the histopathological, clinical, and biological characteristics of invasive tumours [2,3]. As opposed to truly superficial (ie, pTa disease), the treatment of choice for pT1G3 BC has not been defined to date. A secondary resection has been recommended in light of roughly 40% of residual disease in secondary TURB [4,5].

Organ-preserving approaches are successful in approximately 50% of all cases [6], and bacillus Calmette-Guérin (BCG) following TURB has been demonstrated to prolong the interval until recurrence, but not to improve overall survival [7]. However, the efficacy of an organ-preserving approach seems deficient in some cases because 30% of patients require deferred cystectomy (CX) and 30% ultimately die from metastatic disease [7].

Accordingly, early CX has been shown to improve tumour-specific survival rates [8]. Further support for an early aggressive approach is provided by understaging in the first TURB specimen in up to 50% of cases [9,10]. Despite low overall mortality after radical CX (<3%), most urologists prefer a less invasive approach and will resort to CX in recurrent and progressive cases only [11].

To date there has been no randomised clinical phase 3 trial comparing immediate CX with an organ-preserving approach. Various factors have been studied to distinguish between cases requiring early CX and those suitable for organ preservation. No biological markers have proved to be of sufficient prognostic value [12]. Sylvester et al [13] established a scoring system in pTa-1 disease with multifocal disease, concomitant CIS, and tumour size >3 cm as factors predicting high-risk disease. He argued that the treatment of pT1G3 BC should be adapted to each tumour characteristic [13,14], but there are still conflicting reports on the predictive value of these factors [15]. Hurle et al [16] reported only tumour size and coexisting CIS to be correlated with outcome in 51 patients, and Lebret et al [17] found tumour size only, but not multifocality, to predict recurrence and progression in 35 patients. Brake et al [18] found no impact of concomitant CIS in 44 cases, and Pansadoro et al [19] could not establish any predictive value for the number of lesions or associated CIS in a series of 81 patients. To date, no study has been published on the relationship between these factors and clinical outcome in initial or deferred CX. In this analysis we compare the long-term results in patients with initial pT1G3 BC as diagnosed by TURB, and treated with either early CX or initially with an organ-preserving approach and CX upon disease recurrence of the same or muscle-invasive stages, with special regard to clinical risk factors in the initial TURB specimen.

2. Methods

2.1. *Patients and treatment groups*

The clinical and histopathological data of 189 consecutive initial BC staged as pT1G3 between 1995 and 2005 at our institution were reviewed. All cases were treated according to the EAU guidelines on bladder cancer [12]. To enter the analysis, patients had to present with a medical condition justifying major surgery and a combination (≥2 risk factors) of large tumours (>3 cm), multifocal disease, and/or concomitant CIS. Fifty-six percent ($n = 105$) of pT1G3 patients fulfilled the criteria, and all 105 patients entering the analysis were offered early CX accordingly. Of those high-risk patients, 51% ($n = 54$) opted for early CX on average 4 wk following the initial TURB. In contrast, 49% ($n = 51$) of patients had to undergo deferred CX owing to recurring BC. Table 1 provides detailed patient characteristics.

Table 1 – Characteristics of 105 patients after initial TURB undergoing early or deferred cystectomy (level of significance $p < 0.05$, not significant)

	Early CX	Deferred CX	*p* value
No. of patients	$n = 54$	$n = 51$	
No. of male patients	$n = 32$	$n = 30$	$p = 0.72$ (NS)
Median age (yr)	73.5 (range, 36–86)	75.2 (range, 43–84)	$p = 0.21$ (NS)
Multiple tumours $n = 47/105$ (45%)	$n = 23$	$n = 24$	$p = 0.24$ (NS)
Tumour size > 3 cm $n = 77/105$ (73%)	$n = 42$	$n = 35$	$p = 0.09$ (NS)
CIS $n = 48/105$ (46%)	$n = 21$	$n = 27$	$p = 0.18$ (NS)

CX, cystectomy; NS, not significant; CIS, carcinoma in situ.