Quality of life after bladder cancer: a prospective study comparing patient-related Outcomes after radical surgery or radical radiotherapy for bladder cancer


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Q-ABC - Quality of Life After Bladder Cancer; a prospective study comparing patient related outcomes following radical surgery or radical radiotherapy for bladder cancer

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Bladder cancer predominantly affects an older population, a demographic which is growing along with the incidence of bladder cancer [1]. It is the 7th most common cancer in the UK, 4th most common in males, with in excess of 10,300 diagnoses in 2011 and 5081 deaths. This disease and its subsequent treatments result in high morbidity irrespective of outcome which impacts significantly on the quality of life (QoL) of patients and their carers, and has resource implications for healthcare systems.
Approximately twenty-five per cent of patients present with muscle-invasive bladder cancer (MIBC). Open radical cystectomy with urinary diversion or orthotopic neo-bladder formation (ONF) has been considered to be the standard of care, though recent NICE guidance recommends eligible patients are offered radical surgery or radical radiotherapy with concurrent radiosensitizer [2]. Neo-adjuvant chemotherapy (NAC) is recommended, improving overall survival by approximately 5%.

About 1500 radical cystectomies are performed annually in England, an increase of more than 50% over the last 10 years, and most are for MIBC. Improved surgical techniques, enhanced recovery programmes and centralisation [3] have resulted in recently improved perioperative outcomes with 90 day mortality reducing from 5.2% to 2.1% despite the increase in elderly patients undergoing the procedure. Contemporary surgical series have shown 5 year overall, recurrence free and cancer-specific survival rates of 57%, 48% and 67%, respectively [4].

Complications rates following radical cystectomy are relatively frequent in the longer term (over 15 years follow-up) with ureteric obstruction reported in 14%, stomal problems in 24%, bowel problems in 24%, UTI’s in 20% and metabolic derangement (severe metabolic acidosis in 1%). Renal insufficiency developed in 27%, although in this elderly, comorbid population it is difficult to determine how much of this is attributable to the diversion [5]. Continence rates for ONF are high (>95% daytime and 76% nocturnal). In more recent studies, intermittent self-catheterisation (CISC) was required in a minority of patients (10%), with higher rates observed in women [6].

Recent radiotherapy studies, evaluating concurrent regimes with radio-sensitizers, such as chemotherapy or carbogen and nicotinamide, have seen survival outcomes improve and equal results from contemporary surgical series [7, 8]. Unfortunately, a randomised trial directly comparing surgical and radiotherapy outcomes in this disease has not been completed. The CRUK SPARE trial closed early due to poor recruitment and it is unlikely that another randomised study will be attempted. The majority of published data comparing outcomes from these two treatment modalities is between single centre surgical series and radiotherapy results of multicentre randomised controlled trials. Nevertheless, it appears likely that for some patients
these two treatment options confer equivalent outcomes with regard to overall survival [9].

Having two definitive treatment options with equivalent survival end points makes QoL outcomes and health economics essential factors in treatment decision-making for patients, carers and healthcare providers.

Studies evaluating QoL outcomes following radical radiotherapy for bladder cancer are largely limited to small, single centre, retrospective series and some using physician reported or unvalidated questionnaires [10-13]. At the time of assessments most participants are recurrence-free biasing the information collected. Unfortunately comparison between and across published studies is limited by disparate methods and tools used to assess QoL outcomes. Using an unvalidated questionnaire with patients treated with either cystectomy or radiotherapy, Caffo found, with 59/93 (63%) evaluable questionnaires, QoL was higher with bladder preservation due to the absence of a stoma, low incidence of urinary symptoms and better sexual functioning [10]. Similar results were reported in a retrospective study comparing patients treated with radiotherapy, those treated with radical cystectomy and urostomy during the same period and a random general population sample [11]. These data showed 74% (43/58) of the radiotherapy group had little or no distressing symptoms from the urinary tract and better overall sexual functioning (higher rates of sexual intercourse and ability to ejaculate in men) compared to the surgical group. Rate of gastrointestinal toxicity was not significantly different between the two groups. Notably, the degree to which sexual function is influenced in women is less well documented. Perhaps due to some extent because bladder cancer incidence is less in women, though in one QoL study women preferred not to answer the question [13].

Response to radiotherapy is important in determining the impact the treatment has on QoL. Lynch et al compared the QoL of patients with a complete tumour response following radical radiotherapy to an age and sex matched control group. Patients completed the Nottingham health profile and physicians reported urinary symptoms utilising the modified bladder symptom score for haematuria, frequency, nocturia, urgency, dysuria, incontinence and rectal symptoms [12]. Both the physician assessed symptom scores and the patients’ scores from the Nottingham health
profile showed those with a complete response to radiotherapy had little change in their QoL. Zietman et al published comparable findings for 71 patients who were alive and disease-free a median of 6.3 years (range 1.6-14.9) following transurethral resection, chemotherapy and radiotherapy for MIBC [13]. They used a QoL questionnaire validated for prostate cancer, adapted for the study, and included domains for sexual and physical function, global health functional status, and measures of body awareness. Urodynamic evaluation was also performed, but only 31 completed both the QoL questionnaire and urodynamic assessment. Most patients had normal bladder function on urodynamic study. However, from the QoL questionnaire 6% of patients reported flow symptoms, 15% urgency and 19% control problems. Levels of global health related QoL were found to be high despite 11% of women using protective pads and 14% of patients reporting distress from bowel symptoms. One prospective study has assessed bladder function at baseline and then 6-monthly thereafter to 36 months. It found improvement in bladder function following chemo-radiation due to primary tumour control and bladder preservation, with satisfactory bladder function for all patients according to LENT-SOMA [14]. Scores for physical, cognitive, social and emotional functioning, were all high after treatment. The QoL of patients for whom local tumour control has not been achieved have not been investigated yet.

Studies have extensively reported the QoL outcomes following radical surgery for bladder cancer, mainly for comparisons between orthotopic neo-bladder and ileal conduit. A recent review of 21 studies including 2285 patients concluded that patients with an orthotopic neo-bladder had marginally better QoL [15]. Most studies were retrospective, none were randomised, and patients with a neo-bladder were younger and fitter, potentially biasing results. Two reviews concluded that existing studies had not demonstrated superiority for any particular urinary diversion and although overall QoL after surgery remained good, further evidence from prospective studies were needed using validated disease specific health related QoL instruments [16, 17]. QoL after surgery may not be equally as good for women since Gacci et al found that women with a urostomy had lower scores for functional and physical wellbeing, and higher levels of fatigue and appetite loss compared to those with an ONF, though the small (n=37) sample size of the study is limiting [18].
Clearly current comparative data on QoL, psychosocial morbidity, and normal functioning are not adequate to fully inform patients with MIBC making treatment decisions. Furthermore, on a population basis this information is required to enable healthcare providers to commission services appropriately to support these patients. This should lead to improved QoL, reduction in avoidable long-term morbidity and potential financial savings for healthcare services. No studies have included comparison of health economic outcomes and nor has any of the retrospective work included patients for whom local control has failed following radiotherapy and for those who have an upfront cystectomy. Gathering information on fear of recurrence is also important as this disease has high recurrence rates, and anecdotally patients treated for bladder cancer tell us this worry frequently occurs; mixed populations of cancer survivors show 39-87% incur some degree of fear of recurrence associated with greater symptomatology and poorer QOL [19].

In summary, QoL outcomes following treatment for MIBC have not been comprehensively studied despite improved treatment outcomes with the routine use of neo-adjuvant chemotherapy, radiosensitization with chemotherapy and carbogen and nicotinamide. A study of comparative outcomes would assist patients in their decision-making process prior to embarking on treatment. Undoubtedly both treatments significantly impact QoL and normal day-to-day functioning. Strategies to minimise this would reduce distress and improve overall functioning. A recent review of Patient-reported outcome measures (PROMS) and survivorship in radiotherapy patients highlights the importance of these in improving practice, symptom, management and identifying care needs [20]. For healthcare providers an evaluation of the overall impact of different treatment modalities is essential to enable appropriate commissioning of support services which may mitigate long-term morbidity. Moreover this fits with a key goal of NHS Outcomes Framework policy to improve QoL in patients with long-term conditions (Domain 2 of the NHS Outcomes Framework [21]) and emerging international efforts to improve quality of cancer survivor care and was highlighted in the recent NICE guidance [2]. Planning is underway for a prospective non-randomised QoL study using validated patient reported outcomes following the radical treatment of MIBC with the involvement of members of Fight Bladder Cancer, input from the NCRI Psychosocial Studies group, and treating clinicians.
References:


