Current management of muscle-invasive bladder cancer

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Received: 28 October 2011 / Accepted: 14 November 2011

Abstract Management of muscle-invasive bladder cancer (MIBC) has changed little in the last twenty years. The gold standard treatment is still cystectomy, but it has a significant negative impact on quality of life. Bladder-preservation strategies can be used in some cases but patient selection for this approach remains unclear. New chemotherapy and biologic agents in combination with surgery or radiotherapy could improve results and these possibilities are currently under investigation.

Keywords Infiltrating bladder cancer · Transurethral resection of the bladder · Cystectomy · Radiotherapy · Chemotherapy

Background Bladder cancer (BC) is the fourth most frequent neoplasia in males in developed countries after lung, prostate and colorectal cancers. In 2008 there were 139,500 new cases and 51,300 related deaths in Europe. Mortality due to BC in males in Spain is one of the highest worldwide (9 deaths/100,000 people/year) while it is low in women (1.4 deaths/100,000 people/year). Smoking is the main risk factor, followed by exposure to other chemicals such as amines, aniline dyes and nitrites. Urothelial carcinoma is the most common histology.

The treatment of choice for patients with muscle-invasive bladder cancer (MIBC) is radical cystectomy. The bladder-sparing approach as multimodality treatment combining transurethral resection of bladder tumour (TURBT) and chemoradiotherapy (CRT) may be an alternative for highly selected patients. However, no randomised trials have yet been performed to compare these two approaches. Although there is evidence to recommend neoadjuvant chemotherapy before cystectomy, this treatment is markedly underused and the role of adjuvant treatment is uncertain.

This paper provides an update on the diagnosis and treatment of MIBC.

Diagnostic and staging procedures

What diagnostic procedures should be performed?

All patients with BC should undergo a thorough physical examination. Bimanual palpation helps to establish the extent of the lesion in patients with locally advanced disease. Cystoscopy is useful to identify the aspect, tumour size, multifocality and abnormal areas where CIS is suspected, and to determine whether there is macroscopic involvement of the prostatic urethra.
All patients should undergo a complete and diagnostic TURBT to stage and to grade the disease. In patients that have extensive disease or locally advanced disease, a diagnostic TURBT would only be considered before proceeding to surgery and possibly downstaging chemotherapy or radiotherapy. This will depend on the comorbidity and surgical risk. Multiple biopsies of the bladder are mandatory in patients with MIBC since it is important to rule out the presence of CIS in the bladder and in the prostate.

Are prostatic urethra biopsies necessary?

Patients with bladder CIS have a high incidence of CIS in the distal ureter and prostate. At the time of cystectomy, intraoperative sampling of the margins of the ureter and prostatic urethra should be performed in these patients with multifocal disease.

When should we recommend a second TURBT?

A second TURBT is not recommended in patients who undergo cystectomy. If a bladder-sparing approach is considered, a second TURBT is mandatory, since it can decrease understaging and residual disease [1], thus improving the results, whether TURBT is the only treatment [2, 3] or is included in a multimodality treatment.

Treatment

Radical cystectomy

What is the surgical technique currently recommended?

Open radical cystoprostatectomy plus lymphadenectomy is the preferred option as a curative treatment in MIBC [4]. The technique consists of excising the bladder by means of infraumbilical laparotomy. The bladder, prostate and seminal vesicles are removed, including distal ureters. When an orthotopic neobladder is programmed, the anterior urethra, rhabdosphincter and sensory and autonomic nerves can be preserved and thereby improve continence and potency rate.

Minimally invasive techniques for the treatment of MIBC are increasingly being applied in radical treatment. Laparoscopy is the most frequent technique used, followed by robotic-assisted laparoscopic surgery. The potential benefits are reduced blood loss and analgesic requirements. Oncological results seem to be similar but follow-up in studies to date is short. In some series, however, it seems that there is a quicker recovery, shorter hospital stay and fewer complications with the laparoscopic approach [5, 6]. Recent series with more than 500 patients have shown that the number of nodes and positive surgical margin rates are similar to those in open surgery [7, 8].

Should pelvic lymphadenectomy be considered the standard practice in all cases of radical cystectomy?

There is increasing evidence that lymphadenectomy offers advantages in disease-specific survival and is related to the number of lymph nodes removed [9, 10]. The extent of a pelvic lymphadenectomy is still under debate, but a standard lymph node dissection up to the crossing of the ureters in the common iliac artery is mandatory [4, 11].

What should the limits of dissection be?

There are three main forms of urinary diversion after cystectomy: abdominal, urethral and rectosigmoid [4]. Ureterointestinal cutaneostomy, or Bricker ileal conduit, is the most commonly used diversion [12].

Diversions to the urethra or to orthotopic neobladders allow micturition through the urethra and avoid the need for a stoma. Quality of life studies have not reached a definitive conclusion regarding which of the two is the better approach. In urinary diversions, there is a selection bias according to stage, age, comorbidity and surgeon’s experience [12]. The results to date show that if there is no leakage of the cutaneous stoma and if the patient obtains good continence with a neobladder, there is no difference in quality of life. Preservation of the urethra is decided according to the perioperative evaluation of the surgical margin [13]; urethrectomy is recommended to those patients with a positive surgical margin. Either with open surgery or minimally invasive techniques the neurovascular bundles can be preserved and good results can be obtained in terms of potency [6, 14, 15].

The number of procedures per year and the experience of the centre appear to be important factors from the point of view of surgical and functional outcome [12] and operative mortality [16].

Neoadjuvant and adjuvant chemotherapy

Is there sufficient evidence to support neoadjuvant CT?

Although there is strong evidence for the use of neoadjuvant chemotherapy, less than 20% of patients receive preoperative chemotherapy. This discordance could be explained by the difficulties concerning correct presurgical staging, the belief that tumours with limited muscle invasion do not benefit from chemotherapy, and the poor performance status in some patients, making them poor candidates for chemotherapy.

Two large positive phase III trials and a metanalysis support a benefit in survival for selected patients receiving neoadjuvant CT [17, 18]. An update of the results of the BA06 30894 trial that compared neoadjuvant CMV (cisplatin, methotrexate and vinblasting) with cystectomy or radiotherapy alone was recently published and disclosed benefits in the CT arm, where there was a 16% decrease in the risk of death (HR 0.84, 95% CI 0.72–0.99) and 6% increase in 10-