CURRENT ISSUES AND PROSPECTS FOR THE DEVELOPMENT OF SCIENTIFIC RESEARCH

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ANALYSIS OF ENDouroLOGICAL TREATMENT TECHNIQUES OF URINARY BLADDER Tumors

Abstract: Transurethral resection is very important not only for diagnosis and treatment of NMIBC, but also for its management. The application field of transurethral resection includes establishing histological diagnosis, determination of prognostic factors including the tumor stage, complete resection of all detected tumors of urinary bladder. Transurethral resection of bladder tumor (TURBT) is the standard technique for the diagnosis and treatment of non-muscle invasive bladder cancer. This method has also some limitations. One of the limitations is the insufficient assessment of the resection depth. It leads to the necessity of intravesical tumor fragmentation, but its disadvantage is that it limits the histopathological evaluation. In order to improve the treatment outcome for patients with non-muscular invasive bladder tumors, several new techniques such as En-bloc resection were proposed.


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Introduction

A major challenge in healthcare worldwide in both the western countries and in developing countries is the urothelial bladder cancer (UBC), because it represents not only an oncological but also an economical challenge [1,2]. Comparing non-muscle invasive bladder cancer (NMIBC) in patients with detected disease in mucosa (stage Ta, carcinoma in situ) or submucosa (T1), and muscle-invasive bladder cancer (MIBC), the mortality rate is lower in case of NMIBC [4,5].

It is worldwide the 11th most common malignancy. Bladder cancer can be divided into two types: non-muscle invasive bladder cancer and muscle-invasive bladder cancer, hereby the NMIBC makes up about 75% and the MIBC about 25% [6]. Statistically in 2016 the age-standardized incidence rate in case of bladder cancer was worldwide 6.69 per 100000 persons [7].

Transurethral resection of bladder tumor (TURBT)

Transurethral resection is very important not only for diagnosis and treatment of NMIBC, but also for its management. The application field of transurethral resection includes establishing histological diagnosis, determination of prognostic factors including the tumor stage, complete resection of papillary NMIBC [5,8].

Staging is important for an effective treatment in case of bladder transitional cell carcinoma, such as muscle-invasive bladder cancer and non-muscle invasive bladder cancer. They include remarkable different treatment techniques and clinical outcomes. The gold standard is still the transurethral resection of bladder tumor (TURBT) [9].

In oncology the clinical approach to solid tumor of the bladder has several peculiarities [10]. One of the peculiarities is the scattering of the tissue which generates a lot of exfoliated cancer cells. This is the reason why standard technique are not unified. It is still not clear which influence do these floating cells have in the context of out-of field and in-field recurrences [11].

En-bloc resection of bladder tumor

A frequent consequence after TURBT is recurrence. Another important fact is also that tumor can be understaged. In order to solve these limitations, the surgical strategy was technologically optimized e.g., due to new energy sources etc. En-bloc resection is a new approach among surgical techniques. Its principle is based on
circular incision of the mucosa taking in account a safe distance to the lesion, then follows the preparation and resection of the whole tumor, including the underlying detrusor muscle (Figure 1). According to the recent data such a ‘no-touch’ principle represents a technique of a higher quality, decreases surgical radicality and reduces the recurrence rate [12].

The En-bloc resection is a well-tolerated technique and is feasible in application, especially for certain cases. In case of En-bloc the specimen is of high quality and is well oriented, therefore the assessment of tumor stage can be much easier performed by the pathologist [13].

A. Tumor visualization
B. Marking of the resection area
C. Tumor resection
D. Assessment of the post-resection area

Fig. 1. Technique of En-bloc resection (clinical case)
Discussion

Currently, the goal of TURBT, which remains the gold standard in the treatment of non-muscle invasive bladder cancer, is to remove all visible and modified tissues for further study and accurate pathological diagnosis [14,15,16]. The detection of detrusor muscle within the tissue is the most significant factor for postoperative prognosis [17].

In table 1 and table 2 are shown the results of comparative analysis between the En-block bladder tumor resection technique and transurethral bladder tumor resection. These results are based on the literature data from the last years [18]. This analysis was obtained based on the information from 11 articles with the total amount of 1127 patients. Among the years these are divided as follows: from the year 2019 – 3 articles, 2018 – 4 articles and 2017 also 4 articles. Regarding the patients data, the average age of the patients was 55.9 – 69.7 years. Follow-up duration was from 16 months to 96 months. The studies mentioned above were conducted in different countries: China, Egypt, Japan and European countries. In the articles different energy sources were described: monopolar and bipolar electricity, hybrid knife (Hybrid-Knife), Thulium laser (Thulium: YAG), KTP laser and the combination between several methods (Table 1).

<table>
<thead>
<tr>
<th>Year, Region, Author</th>
<th>Energy source</th>
<th>Number (M/F); Age (En-bloc/TURBT)</th>
<th>Tumor diameter (En-bloc/TURBT)</th>
<th>Operation time (En-bloc/TURBT)</th>
<th>Hospital stay (En-bloc/TURBT)</th>
<th>Complication (En-bloc/TURBT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019, Europe, Hurle</td>
<td>Several</td>
<td>78 (51/27); 68 years (En-bloc)</td>
<td>19mm</td>
<td>NR</td>
<td>NR</td>
<td>CD class 1 5.1% (En-bloc)</td>
</tr>
<tr>
<td>2019, Japan, Hayashida</td>
<td>Combined</td>
<td>80 (45/25); 69.7 years/70.5 years</td>
<td>29mm/26mm</td>
<td>18.3/17.3m</td>
<td>NR</td>
<td>CD class 1 (17.9%/19.4%)</td>
</tr>
<tr>
<td>2019, China, Liang</td>
<td>KTP laser</td>
<td>158 (129/29); NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>
Table continuation

<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Technique</th>
<th>Age at Diagnosis</th>
<th>Tumor Dimensions</th>
<th>Duration</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>Romania, Balan</td>
<td>Bipolar electrode</td>
<td>90; 64.7 years/66.1 years</td>
<td>18.2mm/16.9m</td>
<td>2.3 day/3.1 days</td>
<td>RNO (4.4%/11.1%)</td>
</tr>
<tr>
<td>2018</td>
<td>China, Li</td>
<td>Thulium laser</td>
<td>256 (208/48); NR</td>
<td>23.9mm/21.5m</td>
<td>3.1 days/5.2 days</td>
<td>ONR (0%/3.3%), BP (0%/0.83%), CD class 1 (1.5%/2.5%)</td>
</tr>
<tr>
<td>2018</td>
<td>China, Cheng</td>
<td>Hybrid-Knife</td>
<td>183 (95/98); 62.4 years/60.8 years</td>
<td>25mm/28mm</td>
<td>3.5 days/4.5 days</td>
<td>ONR (2.1%/7.1%), BP (9%/2%)</td>
</tr>
<tr>
<td>2018</td>
<td>China, Zhang</td>
<td>Bipolar electrode</td>
<td>82 (61/21); 58.4 years (En-bloc)</td>
<td>24.2mm</td>
<td>3 days</td>
<td>0%</td>
</tr>
<tr>
<td>2017</td>
<td>Egypt, Aboutaleb</td>
<td>Bipolar plasma</td>
<td>46 (36/10); 62.7 years (En-bloc)</td>
<td>17.8 mm</td>
<td>35.4 hours (En-bloc)</td>
<td>Bleeding 6.5% (En-bloc)</td>
</tr>
<tr>
<td>2017</td>
<td>China, Cheng</td>
<td>KTP laser</td>
<td>64 (55/9); 59.4 years/63.1 years</td>
<td>16.5mm/15mm</td>
<td>5 days/5 days</td>
<td>ONR (0%/10%)</td>
</tr>
<tr>
<td>2017</td>
<td>China, Xu</td>
<td>Thulium laser</td>
<td>68 (59/110); 59.5 years/59.7 years</td>
<td>23mm/22mm</td>
<td>5.8 days/6.4 days</td>
<td>ONR (0%/15.9%), BP (0%/6.8%)</td>
</tr>
<tr>
<td>2017</td>
<td>China, Zhang</td>
<td>Monopolar electrode</td>
<td>90 (73/17); 60.7 years/60.8 years</td>
<td>NR</td>
<td>4.1 days/4.2 days</td>
<td>ONR (22%/24%), PVU (5%/8%), CD class 1 (2.5%/4%), CD class 2 (15%/16%)</td>
</tr>
</tbody>
</table>


In average the dimensions of the tumors are from 15 mm to 29 mm. Such values made the En-bloc resection in majority of cases possible (according to the guidelines recommendations – up to 3 cm). In more than 55% cases the tumor lesions were mainly located on the side walls [19]. In two studies data regarding the average resignation of the detected tumors were not presented (Table 1). The duration of the surgical procedures was in average from 13.4 to 74 minutes, but there was no significant difference between the applied surgical techniques (En-bloc vs TURBT). In two studies the data of the of surgical duration were not presented. Regarding the data about the duration of hospitalization it was observed an average of 2.3 – 5.8 days in case of En-bloc resection and 3.1 – 6.4 days in case of transurethral resections.
of bladder tumors. It is evident that there is a tendency to decrease the hospital stay in case of En-bloc resection [20,21,22,23,24,25,26,27].

The data show that among the complications predominate obturator nerve reflex (ONR) and bladder perforations (BP). In three studies the absence of ONR was reported. Such a situation was observed in case of using the laser energy for tumor resection. The percentage of ONR varies between 0% and 24%, but bladder perforations (BP) occur in 0% - 9% of cases. Regarding the Clavien-Dindo complications class I, the percentage of complications varies between 2.5% and 19.4%. Important to mention is that there was lack of a common system of standardized reports of complications, that is why the data do not show an efficient analysis of complications [21,22,23,25,26,28].

Table 2

<table>
<thead>
<tr>
<th>Year, Region, Author</th>
<th>Energy source</th>
<th>pT stage (En-bloc/TURBT)</th>
<th>Detrusor (En-bloc/TURBT)</th>
<th>Recurenta (En-bloc/TURBT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019, Europe, Hurle</td>
<td>Many</td>
<td>Ta 21.79%, T1 73.08%, Tis 5.13%</td>
<td>100% En-bloc</td>
<td>14.1% (overall)</td>
</tr>
<tr>
<td>2019, Japan, Hayashida</td>
<td>Combined</td>
<td>Ta 48.7%/51.6%, T1 46.2%/45.2%, T2 5.1%/3.2%</td>
<td>100% En-bloc</td>
<td>15.4%/19.4% (12M)</td>
</tr>
<tr>
<td>2019, China, Liang</td>
<td>KTP laser</td>
<td>Ta 33.0%/47.1%, T1 67.0%/52.9%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>2018, Romania, Balan</td>
<td>Bipolar electrode</td>
<td>Ta 53.3%/51.1%, T1 46.7%/48.9%</td>
<td>NR</td>
<td>17.1%/27.5% (12M)</td>
</tr>
<tr>
<td>2018, China, Li</td>
<td>Thulium laser</td>
<td>NR</td>
<td>95.6%/83.3%</td>
<td>NR</td>
</tr>
<tr>
<td>2018, China, Cheng</td>
<td>Hybrid Knife</td>
<td>Ta 54.7%/55.1%, T1 45.3%/44.9%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>2018, China, Zhang</td>
<td>Bipolar electrode</td>
<td>Ta 31.7%, T1 62.2%, T2 6.1%</td>
<td>100% En-bloc</td>
<td>20.8% (18M)</td>
</tr>
<tr>
<td>2017, Egypt, Aboutaleb</td>
<td>Bipolar plasma</td>
<td>Ta 30.4%, T1 54.3%, T2 15.2%</td>
<td>NR</td>
<td>15.2% (12M)</td>
</tr>
<tr>
<td>2017, China, Cheng</td>
<td>KTP laser</td>
<td>Ta 41.8%/43.33%, T1 47.06%/50.00%, T2 11.76%/6.67%</td>
<td>97%/80%</td>
<td>8.82%/33.33% (12M)</td>
</tr>
</tbody>
</table>
According to the TNM classification of the tumor’s staging predominates T1, it is found in 45 - 73% of cases and Ta, which is found in 22 - 57% of cases (Table 2). A relevant indicator of quality of resection is the presence of the detrusor muscle in the specimen. So, its presence shows high quality of the resection. Data about the presence of detrusor muscle were given in 6 out of 11 studies. According to these data in four studies which report the results after the post-En-bloc resection the detrusor muscle was present in 100% of cases, and two other studies report about detrusor muscle presence in 97.1% and 95.6% of cases. In comparison, after transurethral resection TURBT detrusor was detected from 54% to 83.3% of cases. Eight out of eleven studies reported information about tumor recurrence. The general recurrence ranged from 8.8% to 33.3% (follow-up of patients for at least 12 months), almost in all studies the recurrence was lower (from 4% to 24, 5%) in groups of En-bloc resection showing the higher efficacy of the En-bloc resection technique [20,21,22,23,25,26,27,28].

In case of En-bloc resection the quality of the specimen increases, the surgical radicality decreases and the recurrence rate is reduced. However, some advantages of the En-bloc resection should be emphasized more precisely, on the one hand it is the extent of incision which is required for lesions in different bladder parts, on the other hand the control of the filling of bladder during surgery. Other important features which should be mentioned is the specimen handling, and also the technique of bladder resection [12].

Conclusions

En-bloc is an important approach for solving the problem of limitations of TURBT. It has also several advantages which ensure its feasible application. However, it is still in discussion which advantages of this procedure will increase its efficacy in clinical practice. Histologically the En-bloc improves significantly the quality of resected specimens. Regarding the associated perioperative morbidity, it
is evident that En-bloc and TURBT do not differ significantly. There are still a lot of challenging questions, like optimal tumor type and resection technique, which have to be answered in order to ensure a wide application of the En-bloc resection.

References:


