REVIEW ARTICLE

Palliative management of malignant upper urinary tract obstruction

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Abstract
Malignancies of the genitourinary tract are diagnosed with increased frequency compared to the past. Currently prostate and bladder cancer account for the majority of urological malignancies. While for prostate cancer recent developments in the management of local and metastatic disease are likely to lead the majority of patients to either cure from the disease or to longer survival time, for bladder cancer advanced disease will unfortunately lead to death within months. However, the common clinical scenario in both prostate and bladder cancer includes, in high incidence, upper urinary tract obstruction in the advanced stages of these malignancies. This coupled with the fact that average life expectancy in the western world is increasing, will result in a significant patient population with either advanced, non-curable disease or with problems related to the received therapeutic surgical or medical interventions. There is no doubt that in both circumstances the room and role of palliation therapy is increasing. The care of patients with advanced urologic malignancies requires a multi-disciplinary effort from physicians of many specialties under the guiding role of the treating urologist. This review focuses on currently available palliative therapeutic options for upper urinary tract obstruction in the setting of patients with advanced malignancies of the urinary tract, as recently significant advancements have been witnessed in this field. Hippokratia 2014; 18 (4): 292-297.

Keywords: Urologic malignancies, upper urinary tract obstruction, ureteral stents, nephrostomy, palliative management

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Introduction

Palliative care plays an important role in the overall care of patients with cancer. A patient is considered for receiving palliative care when he or she is not a candidate for any form of curative treatment or does not wish to accept the related morbidity. The goal of palliative care is to provide comprehensive relief from disease-related or treatment-related conditions or side effects in order to achieve the highest possible quality of life and survival prolongation. Palliative care has been consistently shown to improve quality of life in cancer patients by addressing the harmful effects of pain and other symptoms[1].

Malignancies and upper urinary tract obstruction

According to recent data, nearly one-half (45%) of cancer survivors are aged 70 years or older, while only 5% are younger than 40 years. Moreover as of 2022 it is estimated that cancer survivors will increase to nearly 18 million[2]. Urological malignancies are affecting people of older age, are not usually upfront lethal, especially prostate cancer, and as a result, patients with urological malignancies often live many years with their disease. However upper urinary tract obstruction may be the results of numerous malignancies apart from those originating from the genitourinary system including colorectal cancers, gynecological malignancies and primary retroperitoneal tumors.

Prostate cancer (PCa) is the most frequently diagnosed cancer in men worldwide and the second leading causes of death from malignancies in men[3,4]. The incidence of PCa diagnosis in European countries is on the rise, partly due to the increased implementation of prostate cancer screening[5]. Despite advances in early detection of prostate cancer, as many as 10% of patients present with or develop symptomatic locally advanced prostate cancer with upper tract obstruction as their main symptom[6]. Although it is not easy to precisely estimate the incidence of hydronephrosis in the course of other malignancies, there is evidence that hydronephrosis and elevated creatinine develops in up to 38% of patients with locally advanced colorectal cancer[7].

Upper urinary tract obstruction, from either benign or malignant causes, is a relatively common condition for practicing urologists. The constant evolutions in endourology have effectively facilitated minimally invasive management of upper-tract obstruction. Questions arise regarding the optimal means to relieve obstruction, the benefits and drawbacks of each technique, regarding its efficacy and impact on patients' quality of life.

Hydronephrosis caused by extrinsic compression from tumor or retroperitoneal lymph node mass is a usual situation in the course of advanced malignancies. The majority of these cases are of urologic, gynecologic or gastrointestinal origin, and the situation may be aggravated by periureteral fibrosis, a long-term adverse event of previous chemotherapy and radiation therapy. The cause of obstruction may be invasion-infiltration of the ureters by tumor (cervical, bladder, prostate, or colorectal cancer), extrinsic compression by a retroperitoneal primary or metastatic neoplasia, or scarring, adhesions, and luminal ureteral strictures resulting from radiotherapy or chemotherapy (Table 1). Upper urinary tract obstruction, especially bilateral hydronephrosis, is considered a prognostic indicator of morbidity, disease progression and reduced survival in cervical and gastrointestinal cancer[8-10].

Table 1: Causes of upper urinary tract obstruction related to malignancies.

Causes of upper urinary tract obstruction related to malignancies
• Malignancies of the urinary tract (bladder cancer, prostate cancer, TCC of the upper urinary tract)
• Malignancies of the female reproductive system (endometrial cancer, cervical cancer)
• Malignancies of the gastrointestinal tract (gastric cancer, colorectal cancers)
• Primary and secondary malignant retroperitoneal tumors
• Retroperitoneal fibrosis (from chemotherapy, radiation)
• Anastomotic strictures following urinary diversion
• Cancer- related lymphadenopathy

There are absolute as well as relative indications for reversing an obstruction. Obstruction should be certainly relieved in cases of unremitting pain as well as in cases of febrile upper urinary tract infection (UTI) irrespective of disease stage or estimated survival time. In the case of life-threatening renal insufficiency from upper urinary tract obstruction, the decision to relieve obstruction or not, should be weighed against the prognosis of the individual, the impact of the scheduled intervention on quality of life and, of course, patients' preferences[11].

There is evidence that palliative urinary diversion will prevent deterioration of renal failure and may result in a survival benefit[12,13]. For patients with end-stage cancer, however, although palliative urinary diversion may prolong survival for weeks or months, this gain should be balanced against the anticipated effect on quality of life after diversion. Given that the median survival for these patients usually does not exceed 1 year, prolonging survival by preventing death from uremia may come with the price of reduced quality of life because of pain, fatigue, or other sequelae of advanced metastatic disease[14]. On the other hand, relief of upper urinary tract obstruction will likely lead to decreased creatinine levels and thus permit the use of chemotherapy for the treatment of the underlying malignancy[15-17].

Still for the majority of cases, upper urinary tract decompression and maintenance of ureteral patency even as a palliative measure is mandatory. Options for upper tract decompression include percutaneous nephrostomy, retrograde stenting and open urinary diversion.

Ureteral stent or nephrostomy tube?

The two more favored options for decompression of an obstructed collecting system in cancer patients are retrograde or antegrade insertion of an indwelling ureteral stent or placement of a percutaneous nephrostomy (PCN).

Although there has been extensive debate on the risks and benefits of insertion of ureteral stents and placement of nephrostomy tubes, it is not clear which modality provides maximal benefit and for which patients. The fact that there are no guidelines for the management of malignant ureteral obstruction accounts for the certain disparity in practice patterns among urologists and medical oncologists, as has been shown in a survey[18].

Indications

A trial of retrograde stent placement is considered by many urologists as first-line treatment option for patients with extrinsic ureteral obstruction of malignant origin. Retrograde ureteral stent insertion and nephrostomy catheter placement are performed under fluoroscopic guidance with patients under local anesthesia, monitored sedation, spinal, or general anesthesia. In case that the retrograde placement of a stent is successful, patients usually have periodic endoscopic stent change every 3 to 12 months[8]. Retrograde stent placement might be the preferred initial approach in cases where nephrostomy is anticipated as technically difficult because of extraordinary body habitus or in patients with a solitary functioning kidney due to the small but present risk of severe hemorrhage[19]. The presence of severe coagulopathy is a relative contraindication to PCN[20]. One can argue that ureteral stent is less invasive than nephrostomy and probably better tolerated, suggesting that it may be more advantageous especially in view of the limited life expectancy of patients with advanced malignancies[21,22].

Placement of a nephrostomy tube may be the first option in cases of ureteral obstruction from cervical, prostate, or colorectal cancer. PCN should also be the preferred option in cases of significant involvement of the bladder by a prostatic or bladder malignancy, where attempts for identification of the ureteral orifices usually fail[23,24]. Other contraindications to retrograde stent placement include gross hematuria or difficulty in reaching the bladder due to previous surgery or anatomic anomalies[23-25]. PCN may also be more effective in relieving upper-tract obstruction in cases of extensive peritoneal carcinomatosis from gastrointestinal malignancies and in cases where obstruction is complicated by pyonephrosis with thick purulent material filling the renal pelvis. In these cases a large bore nephrostomy tube provides better chances of drainage compared to internal stents. Drainage failure of ureteral stents in advanced pelvic carcinomatosis has been attributed to the absence of long-segment ureteral peristaltic movement because peritoneal carcinomatosis induces obstruction along the entire ureteral length[26].

Efficacy

PCN placement has remarkable technical success rates (96% to 100%) in relieving upper urinary tract obstruction[27,28]. Regarding stents, there is a significant improvement in the success rates with retrograde stent insertion being technically successful in around 85% of cases according to results from recent series[21,24,28,29].

Still, failure of ureteral stents to maintain a patent upper tract is common for patients with malignant obstruction. Cancers originating from the gastrointestinal tract, poor performance status and severe hydronephrosis have been identified as independent predictors of stent failure[30].

There are certain parameters inherent to malignancies to be held responsible for the higher rate of stent failure in this setting. Stent encrustation and tumor growth through the stent are usual causes of stent obstruction resulting in more frequent stent change or resolving to PCN[26].

Quality of life after palliative urinary diversion

Despite the technical improvements in stents design and compatibility, neither nephrostomy tube placement nor internal stent placement are able to significantly prolong median overall survival for patients with advanced cancer[13,27]. Therefore, the issue of quality of life and its relation to the type of urinary diversion is gaining significance. When quality of life is addressed, one should take into account the benefits and advantages of each intervention. Relevant to PCN, early results showed marked deterioration in quality of life of patients with malignant obstruction[31].

Shekarriz et al evaluated the performance status of patients with advanced malignancies following urinary diversion by either stent or nephrostomy, using the modified Karnofsky performance scale as an indirect tool of quality of life. The results showed that the overwhelming majority of patients remained on a poor performance status after diversion, irrespective of the means of diversion. Overall, patients were found to have spent almost half of their survival time after intervention in the hospital, while 15% never left the hospital after the procedure. In total, 68% had either minor (63%) or major (5%) procedure-related complications. Karnofsky scores revealed that performance status did not change for the majority of patients despite palliative diversion[12].

Despite the high technical success rate of PCN, studies have shown a high incidence of complications that are associated with the long-term management of PCNs, resulting in inferior quality of life compared with internal stents. In recent studies, tube dislodgement or blockage occurs in 10% to 19% of patients with malignant obstruction, with the need for replacement and possible hospital stay adding to the compromised quality of life of these patients[16,28]. Other problems that can contribute to poor quality of life after PCN are urinary leakage, skin excoriation and inflammation at the nephrostomy exit site[10].

On the other hand, there are reports demonstrating a positive effect of urinary diversion on quality of life with either nephrostomy or stent. Gasparini et al reported an almost 1.5 year of average survival after diversion in a group of 22 patients. Seventy seven percent of patients were discharged home after the procedure and spent 86% of their remaining survival time at home[32]. Kanou et al found diversion, by means of a stent or a nephrostomy catheter, to have a meaningful effect on quality of life for approximately two-thirds of patients[24].

The issue of quality of life for cancer patients, however, is multifactorial, and in the absence of a validated quality-of-life assessment tool, there is a need for prospective trials that directly compare PCN with retrograde stent placement regarding complications and their impact on overall quality of life.

Metallic "tumor" stents

The introduction of metallic stents for the management of malignant ureteral obstruction aimed at addressing some of the problems and limitations encountered with the use of double-J stents. In the setting of malignant ureteral obstruction (MUO) there is a need for stents that can be left *in situ* for prolonged periods providing efficient drainage of the upper urinary tract with minimal morbidity. The theoretical advantages of metal stents over polymer ones include reduced encrustation, improved tensile strength and stability, prolonged stent indwell time, and better flow.

A variety of metallic alloys, designs, lengths and configurations of metallic ureteral stents have been used. The self-expandable elastic mesh stent [Wallstent™ (Endoprosthesis, Boston Scientific, USA)], made of stainless cobalt, was introduced for use in ureteral stenosis. Overall, although Wallstents may offer a salutary solution to upper tract obstruction, their use was compromised mainly by its low patency rates requiring additional endourologic interventions (coaxial stenting, balloon dilation)[17,33].

Self-expandable mesh stents

Self-expandable mesh stents [Memokath™ (Pnn Medical, Switzerland), Uventa™ (Taewoong Medical, South Korea)] were introduced in upper tract obstruction in an effort to overcome the problems of encrustation, urothelial hyperplasia and difficult removal that were common with the self-expandable stents. In theory, the Memokath was ideal as it has shape-memory, a low propensity for encrustation and a tight spiral configuration designed to minimize tissue ingrowth.

In real life though, insertion or removal of a Memokath stent can be problematic due to the need for precise estimation of the length and location of the stricture for correct stent placement. Also stent migration and encrustation did not cease to be troublesome issues[34]. Results were more encouraging with the use of the Uventa™ stent, a double-layered self-expandable mesh stent made from polytetrafluoroethylene. Two recent studies with 54 and 18 patients with MUO respectively showed an overall success rate, defined as no obstruction and no need for additional intervention, of 82%-100% with the more frequent complications being flank pain (15%) and transient hematuria[35,36].

Covered metal stents

A solution at that time was the introduction of covered metal stents using various biocompatible materials, in an effort to prevent tissue ingrowth and minimize urothelial trauma. The rationale was that stents covered with various biocompatible materials in the absence of side holes would potentially limit the ingrowth of hyperplastic tissue into the ureteric lumen, thereby improving patency. In clinical practice, initial results were not enthusiastic. The Passager™ (Boston Scientific, USA) stent, a flexible stent, externally covered with ultrathin woven polyester fabric, demonstrated a high failure rate mainly due to bladder migration. Failure was attributed to increased ureteral peristalsis and also the covering of the stent was "accused" of preventing adequate stent adherence to the ureteral wall resulting in stent migration[37].

A nitinol stent (Hemobahn Endoprosthesis, Gore WL and associates, Flagstaff, USA) completely covered with expanded PTFE has also been used for malignant upper tract obstruction[38]. The Hemobahn endoprothesis is internally covered by polytetrafluoroethylene (PTFE) so that the outer metallic mesh has direct contact with the urothelium for better anchoring of the stent to the ureteric wall. Although the preliminary results were better compared to the Passager stent, stent migration still occurred in 22% of cases and was resolved by the placement of a second stent[39].

Despite certain advancements, all of the above metallic stents share, to a greater or lesser extent, some of the following drawbacks: a) they are short semi-permanent stents, b) migration is still a problem due to their size and limited adherence to the ureteral wall, c) long-term patency may require placement of additional stents or other interventions[32,40].

Coiled metal stents-The Resonance™ stent

Stent design, properties and technique of placement

A new design metallic ureteric stent has been introduced for the management of ureteral obstruction in an attempt to overcome problems such as the low primary patency rate and the high risk of stent migration. The 6 French gauge (F) Resonance™ (Cook Medical, USA) metal stent is designed in the style of an indwelling full-length ureteral stent with conventional pig-tail ends, but no end holes. It is constructed of Multiphase™ (MP35N®) alloy, a composite of nonmagnetic nickel-cobalt-chromium-molybdenum, possessing a combination of ultrahigh tensile strength and excellent resistance to corrosion. Its super elastic properties provide tremendous power as well as flexibility[41] (Figure 1).

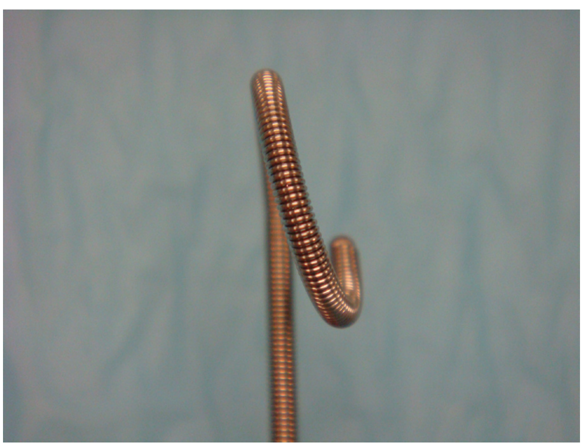

Figure 1: The coiled closed end of the metallic Resonance™ stent.

The technique of placement of the Resonance™ stent differs from that of conventional ureteric stents. The absence of end-holes makes impossible the placement of the stent over a guide-wire, and the flexibility of the stent discourages the forcible pushing of the stent through a ureteral stricture. For these reasons the Resonance ™ stent is introduced through an outer sheath, although insertion with the aid of a ureteral access sheath has been recently reported[42].

As the Resonance™ stent has no end-holes urine drainage is accomplished by a combination of extraluminal and intraluminal flow. Urine drains primarily around the outer aspect of the spiral coiled metal; however in cases of increased pressure within the upper tract, urine enters the internal lumen of the coil[43]. The unique properties of the particular alloy of the Resonance™ stent should prevent hyperplastic tissue ingrowth and encrustation, and improve the stent's biocompatibility. A recent study with the use of electron microscopy and spectroscopy has confirmed the lack of epithelial tissue ingrowths and durability of the Resonance ™ stent[44].

Experience with the Resonance™ stent

Experience with the insertion of Resonance™ stents in a series of patients with malignant ureteral obstruction was recently reported. Seventeen stents were antegrade placed in fifteen patients with various malignancies prior to chemotherapy. Three of the seventeen stents had failed in the first day, as was evident by nephrostograms and renal function deterioration. All three stents were placed in patients with bulky pelvic disease and all of them were subsequently maintained on external drainage by percutaneous nephrostomies. The rest of the stents were functioning properly with no evidence suggesting stent blockage before change of the stent, usually every 6-12 months. Encrustation was minimal in all cases where the stents were changed after some months[45].

Liatsikos et al recently published their experience on the mid-term effectiveness (8.5 months of follow up) of the Resonance™ stent in 25 patients with malignant ureteral obstruction. The technical success rate was 100% and all stents remained patent during the follow up[46].

Studies with longer follow up have somewhat lessened the initial excitement about the effectiveness of the Resonance™ stent. In the study from Durham, from a total of 37 stents placed in 25 patients with malignant ureteral obstruction, 12 (35%) failed. Relapse and/or deterioration of hydroureteronephrosis and rising creatinine, were the most common signs of stent failure. Patients with prostate cancer invading the bladder, were found to have a significantly higher risk of stent failure. According to authors, the failure rate with metallic stents was not significantly better than those observed with the use of traditional polyurethane-based stents in malignant ureteral obstruction[47]. Similar results (25% failure rate) were reached in the study by Wang et al, in 15 patients with malignant extrinsic ureteral obstruction. The authors identified previous radiation as risk factor for stent failure[48].

A retrospective study of 117 stents, inserted in 79 patients with malignant ureteral obstruction, identified old age and high serum creatinine as predictors of Resonance™ stent failure. The study showed that cancers of the lower gastrointestinal tract were associated with longer patency rates[49].

A retrospective study on 20 patients found the Resonance™ stent to demonstrate excellent patency rates in cases of benign and malignant obstructions, with the exception of patients that received radiotherapy (50% patency rate)[50]. Also the Resonance™ stent seemed to be financially advantageous compared to traditional stents in the long-run[51].

Although the reported results of current research on the effectiveness of the Resonance™ stent are contradictory[52] there is evidence that it holds promise for the effective management of patients with malignant obstruction of the upper urinary tract.

Stents of the future

New generation metallic stents and metallic drug-eluting stents[53], aiming at reducing the hyperplastic reaction, are the near future. These new stents include the Passage™ (Prosurg Inc, California, USA) 7F metallic coil stent and the Snake™ (Prosurg Inc, California, USA) stents. The Passage stent is a flexible metallic coil stent, with a spiral winding configuration with central lumen that allows insertion of the stent using the guidewire and pusher technique.

The Snake gold-plated, metallic spring coiled ureteral stent (6F, 7F) has flexible pigtails and is covered with biocompatible polymer tubing. In contrast to the Resonance stent which is tightly coiled around a stainless steel guidewire and closed at both ends, these stents are less tightly wound and open at both ends.

These stents have been recently tested for coil strength, tensile strength and resistance to extrinsic compression. The Snake 6F stent was the one having the lowest tensile strength followed by the Passage and Snake 7F stents. The elastic modulus, required to cause extrinsic compression, was highest for the Snake 6F stent compared to that of the Passage and Snake 7F stents. A low tensile strength together with a high coil strength are important for prevention of stent migration while a high resistance to extrinsic radial compression is vital for preventing re-obstruction due to tumor ingrowth or extrinsic stent compression[54].

In addition, authors found that the increase of stent diameter of 1F weakened the resistance of radial compression. Therefore in situations where a metal stent is used for alleviation of ureteral obstruction, a 6F stent may be more effective in sustaining ureteral patency over a 7F stent, where radial compression is the greatest threat[50].

Conclusions

In advanced and non-curable disease physicians and patients should have an open discussion about personal goals, life priorities, and available resources for palliation of symptoms. Palliative care should be a standard part of every urologist's practice, as urologists are dealing with malignancies with limited options for cure (i.e. metastatic renal cancer) or long survival time after potentially curative treatments, like in prostate cancer. Relieving upper urinary tract obstruction caused by malignancy is a demanding and challenging situation for both physicians and patients alike. Proof of that, is the constantly evolving landscape of stents relating to their design, materials and properties, in an effort to adapt to the increased patient and physician needs and expectations. There is little doubt that in the future the problem of managing malignant upper tract obstruction will be dealt with by means of stents that would be easier to place, harder to occlude, and less troublesome for the patients.

Conflict of interest

Authors declare no conflicts of interest.

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