Lower Urinary Tract Dysfunction after Radical Hysterectomy for Cervical Cancer

Abstract

Despite effective screening, cervical cancer continues to be a major public health problem among women. Radical hysterectomy represents the cornerstone in the management of localized cervical cancer especially in young women. Lower urinary tract dysfunction (LUTD) represents the most common complication after radical hysterectomy with a substantial negative impact on quality of life of survivors. Most patients with cervical cancer treated with radical hysterectomy receive postoperative bladder care at gynaecology departments and urologists are rarely confronted to patients in the post-operative phase. The etiologic factors and the natural history of LUTD following radical hysterectomy are partially elucidated. Furthermore, effective treatment remains elusive. We performed a PubMed and Medline literature search using the keywords: radical hysterectomy, cervical cancer, and these two terms in combination with urinary dysfunction or bladder dysfunction in order to analyze the evidence on LUTD following radical hysterectomy. Emphasis will be placed on the symptoms as well as their management to prevent upper tract deterioration and to improve quality of life.

Introduction

Cervical cancer is the third most common cancer in women worldwide, with about 530,000 new cases and 275,000 deaths reported annually [1]. Cervical cancer is a major public health problem among women when considering that it affects women < 45 years more than the other major cancers [2]. Radical hysterectomy is the treatment of choice for localized cervical cancer especially in young women. Survival rates following surgery are good reported to be > 85% in contemporary series [3]. These results draw attention to the quality of life of survivors [4]. Radical hysterectomy is associated with early and late lower urinary tract dysfunction (LUTD), sexual dysfunction and to a lesser degree rectal dysfunction that alter significantly the quality of life of survivors [5,6]. LUTD is the most often studied and the best documented type of morbidity after radical hysterectomy. However, there is a wide variation in the incidence of LUTD among different studies. The etiologic factors and the natural history of LUTD following radical hysterectomy are partially elucidated. The present report is a synthetic overview of the literature on the evidence for LUTD after radical hysterectomy for cervical cancer. Preventive measures as well as urologic after cares are also analyzed.

We performed a PubMed and Medline literature search using the keywords: radical hysterectomy, cervical cancer, and these two terms in combination with urinary dysfunction or bladder dysfunction. Significant results and citations were reviewed manually by the authors.

Lower urinary tract symptoms following radical hysterectomy

Lower urinary tract symptoms (LUTS) after radical hysterectomy include a wide range of complaints and physiological phenomena. They are classified as early and late dysfunctions [7]. In the early post-operative phase, LUTS are common after removal of the urinary catheter, reported in 70 to 85% of patients [8-10]. The duration of bladder catheterization is variable among different studies ranging from as early as the second postoperative day to one month after the operation [11,12]. This wide range in the literature is due to different surgical technique, personal preferences and variable policy of every centre. After removal of the bladder catheter, urinary retention is rare reported in 0 to 10% of cases [13-15]. In the first days to weeks after radical hysterectomy, voiding symptoms associated with sensory loss are the major complaints: slow or intermittent stream, splitting, or spraying of the urine stream, hesitancy, and abdominal straining to void. Post-micturition symptoms such as dribbling and feeling of incomplete emptying are also common. Dysuria, chronic urinary retention, overflow incontinence are the hallmark of the voiding dysfunction. The second major complaint is incontinence [16,17]. The most common type of incontinence is the stress urinary incontinence, followed by mixed urinary incontinence [7]. Incontinence is exacerbated by low bladder compliance [16,17]. Despite the fact that incontinence is protective against upper tract deterioration because high leak-point pressures result in reflux and hydronephrosis, it is a major cause of devastating quality of life [18,19]. The incidence of stress urinary incontinence 6 weeks after surgery is 48–53%, dropping to 30% at 3 months and remaining relatively constant thereafter [10,20]. Around 15% of women seek further medical treatment for their urinary incontinence 12 months after treatment [21]. On urodynamic studies, significant reduction of bladder compliance and a significant reduction of maximal urethral pressure at 3–6 months postoperatively were documented [22,23]. The residual volume tends to increase at 2 and 6 weeks after surgery [22]. At uroflowmetry, the mean flow rate and the maximal flow rate showed a reduction at 2 weeks, 6 weeks, and 3 months after surgery [22,23]. Electrophysiologic recordings showed a prolonged pudendal nerve motor latency at 2 and 6 weeks; the pudendal nerve motor latency returned to baseline levels at 3 months [22]. Recently, three comparative urodynamic studies carried out in patients who underwent type 3–4 nerve sparing radical hysterectomy showed no significant changes compared to...
preoperative urodynamic evaluation [24-26]. Spontaneous recovery of bladder function is generally to be expected within 6–12 months after surgery [27]. However, permanent dysfunctions beyond 6–12 months are reported in 30 to 50% of studies [28-30]. Long term LUTD are mostly storage LUTS (increased daytime frequency, nocturia, urgency, and urge incontinence) but 50% of these patients seek medical treatment for their symptoms 1 year after the operation [20]. It seems that cancer patients deal with urinary symptoms better than non-cancer patients given the relatively high level of distress that is usually present regarding their underlying malignant disease [31].

It is important to note that, in cancer patients, functional complaints manifest, generally, at long-term intervals. A study by Chuang et al. showed that the mean interval from radical hysterectomy to urology consultation was 11.3 +/- 9.5 years on the complaints manifest, generally, at long-term intervals. A study [20]. It seems that cancer patients deal with urinary symptoms better LUTD are mostly storage LUTS (increased daytime frequency, nocturia, urgency, and urge incontinence) but 50% of these patients seek medical treatment for their symptoms 1 year after the operation [20]. It seems that cancer patients deal with urinary symptoms better than non-cancer patients given the relatively high level of distress that is usually present regarding their underlying malignant disease [31].

The time to recover postoperative bladder function is variable in the literature. This disparity stems from variable evaluation and definition of bladder function, different operation techniques and different surgical approach. The vast majority of the studies based their evaluation method to assess bladder function recovery on urinary catheter withdrawal and/or PVR volume. Few studies used preoperative and postoperative complete urodynamic study to evaluate bladder function [22,23,26].

Structural basis of LUTD following radical hysterectomy

The pathogenesis of LUTD is not completely understood and actually debated. Accidental damage to the pelvic autonomic nerves during radical hysterectomy is thought to be the major cause [35]. Voiding disorders are the result of impaired modulation in the pelvic plexus, and the resultant motor and sensory impairment of the detrusor. The result is a failure to trigger detrusor contraction and urethral relaxation which leads to detrusor hyperactivity and a non relaxing urethral sphincter [33,34]. The nature of the surgical damage appears to be decentralization rather than a complete denervation and bladder dysfunction may be due to the unmasking of intrinsic detrusor activity, characterized by loss of β-adrenergic innervations with subsequent α-adrenergic hyperinnervation, or due to the impact of residual sympathetic innervations [36-38]. The significant decrease of the maximal urethral closure pressure encountered in the early postoperative period could be attributed to the damage of the pelvic plexus and pudendal nerves with loss of perirethral tone [36]. The loss of sympathetic adrenergic stimulation may have an excitatory effect on parasympathetic transmission to the detrusor muscle during urine which could contribute to the characterization of urinary stress incontinence and detrusor overactivity and incontinence after radical hysterectomy. In a recent study, Axelsen et al. confirmed the crucial role of the urethral sphincter mechanism [30]. They had reported no differences in urodynamic findings between continent and incontinent women after radical hysterectomy except for an overall difference in the intraurethral pressure [30]. Urodynamic correlate between the severity of the incontinence and reduction of bladder compliance had been documented after radical hysterectomy [37]. Spontaneous recovery of bladder function is generally to be expected within 6–12 months after surgery [20,27]. The mechanisms of spontaneous recovery are complicated, probably due to plasticity reorganisation that occurs at multiple levels in the central and peripheral nervous system in response to peripheral injuries [36]. In a feline model, ablation of the pelvic plexus with early widespread degeneration of intrinsic axons and muscle cells was followed after 10 weeks by a period of restitution of cholinergic axon terminals, increase in adrenergic and coepitderic axons, and muscle cell regeneration [36]. In some cases, increased resistance at the bladder neck and hypocontractility of the detrusor will result in straining to void. Furthermore, because loss of normal sensation of bladder fullness, patients will rely on substitute sensation such as fullness in the abdomen or pelvis or vague feeling of discomfort that they gradually learn to associate to a full bladder. It is noteworthy to mention that functional changes to the bladder and urethra alter the quality of life. In addition, they can affect the upper tract causing deterioration in kidney function [28,29]. High post void residual urine and high intravesical pressure during the storage phase could lead to secondary vesicoureteral reflux and hydronephrosis. Moreover reflux may drive pathogenic bacteria into the upper tract causing pyelonephritis and renal scarring. Factors that predict upper tract deterioration are decreased bladder compliance, increased detrusor leak point pressure and acontractile detrusor [16,19].

Prevention and management of LUTD following radical hysterectomy

Close cooperation between the gynaecologists and the urologists before and after radical hysterectomy is an essential prerequisite of good practice for prevention and management of post-operative LUTD. In practice, unfortunately, multidisciplinary management is not well offered to the patients in a timely way even in high centre volume. In general, there are three principles for managing LUTD following radical hysterectomy. First, a thorough urologic preoperative evaluation is mandatory to detect at risk situations for post-operative LUTD in order to inform the patients for the risks of post-operative disorders. Furthermore, Lin et al. showed that only 17% of patients with cervical cancer had normal urodynamic findings before radical hysterectomy [39]. A complete history, clinical examination and if needed a complete urodynamic assessment will help physicians to monitor these patients in the post-operative period. Comparison of preoperative and postoperative evaluation will elucidate the consequences of the operation on lower urinary tract.

Second, minimizing injury and tissue trauma to the pelvic autonomic innervations is one of the principal aims of contemporary surgery in order to prevent postoperative LUTD. All studies comparing nerve sparing techniques to standard radical hysterectomy yielded encouraging results in respect of postoperative LUTD [40-46]. Recently, a meta-analysis demonstrated a lower rate of LUTD in the nerve sparing group compared to the conventional radical hysterectomy group [47]. However, there is no standard approach and review of the literature highlights the lack of consensus in several technical aspects of nerve preserving radical hysterectomy. Adaptation of the extent of resection in accordance with tumour-related and patient related risk factors in each individual patient is mandatory. In general, there are two schools of thought: those who focus their nerve sparing approach on the cardinal ligament, and
those who believe that a limited dissection of the uterosacral ligament is more important [48-51]. Recently, a quantitative analysis of the components of the uterosacral ligament had showed the complex location of the neurovascular bundles. The content of autonomic nerve tissue was significantly higher in the deep portion and the sacral section whereas the lymphatic vessels were significantly greater in the mediastinal surface and in the cervical section [52]. It is noteworthy to mention that nerve sparing approach should not compromise oncological outcomes that remain the primary objective of the surgery. Surgeons need to weight the balance of benefit and risks associated with the extent of their procedure in order to reduce early and late LUTD. Iatrogenic injury to the bladder and ureter should also be avoided because it could interfere with bladder recovery.

Third, close monitoring of lower urinary tract function and adequate urological management of LUTD are mandatory to prevent upper urinary tract dysfunction, and to improve the quality of life of these patients. The best treatment option for bladder emptying and significant PVR volume is clean intermittent catheterization [53]. Abdominal straining to facilitate emptying the bladder is not recommended, as it leads to increased bladder pressure, increased risk of vesicoureteral reflux and pressure propagation to the kidneys, potentially resulting in renal damage in the long term. Voiding without abdominal pressure enhances recovery of bladder function after radical hysterectomy [29]. Adequate postoperative bladder care can help to restore bladder function within 12 months of surgery [29]. The daily frequency of clean intermittent catheterization is dependent on the residual urine volume and occurrence of spontaneous micturition. A permanent indwelling or supra-pubic catheter should be avoided as long as possible as these can lead to complications such as urinary leakage, untreatable infections, bladder stones, fibrotic bladder and bladder carcinoma. Recently, a neuromodulation of the superior hypogastric plexus yielded encouraging results in patients with bladder atonia secondary to pelvic surgery; 3 patients out of 4 were able to partially void or empty their bladder after laparoscopic implantation of a neurostimulator [54]. However, these results were not confirmed in another study [55]. Overactive bladder following radical hysterectomy is difficult to manage. Parasympatholytic drugs are usually ineffective but are tried as a first line therapy and there are no studies evaluating β-agonists for treating bladder hyperactivity after radical hysterectomy [56]. Testing intravesical injection of botulinum toxin, in a clinical trial, for overactive bladder following hysterectomy would also be interesting. In a novel study, Plotti et al. demonstrated a statistically significant improvement on symptoms score of eight patients with refractory overactive bladder after radical hysterectomy treated by a sacral neurostimulation [55]. The overall success rate (87.5%) was similar to the success rate of neuromodulation in general population [57].

For urinary stress incontinence, the first choice of treatment is a midurethral tension-free sling. Performing a mesh sling after radical hysterectomy can be a challenging procedure, with high risks of complications. Less-invasive treatment alternatives such as bulking-agent urethral-injection-therapy could be valid options for these patients [58].

Conclusion

LUTD is the most common complication after radical hysterectomy and it alters significantly the quality of life of the surviving patients. Early post-operative LUTS are common and impose a close urologic care. Persistent late changes alter significantly quality of life and could be deleterious on the upper urinary tract. The structural bases of pathophysiology are partially elucidated. Experimental and clinical studies are needed to understand the neurologic alterations as well as the anatomical changes responsible of LUTD following radical hysterectomy. Effective treatment of postoperative LUTD following radical hysterectomy remains elusive. Nerve sparing radical hysterectomy yielded encouraging results in regard of preservation of bladder function. However, limiting resection should not compromise oncological outcomes and long term oncologic safety should be verified in large randomized controlled trials.

Conflict of Interest

The authors, Marc Zanaty, Alexandre Pelletier, Roland van Velthoven and Fouad Aoun declare that they had no conflict of interest.

References


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