



Editorial and Rebuttal from Authors

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Morbidity from Pelvic Lymphadenectomy in Men Undergoing Radical Prostatectomy

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As is true for the surgical treatment of many other cancers, there is an increasing interest in determining the value of a meticulous pelvic lymph node dissection in prostate cancer patients undergoing radical prostatectomy. Every extended surgical procedure carries additional risks for complications that must be weighed against the potential benefits.

In this issue of *European Urology*, Briganti and coworkers [1] analyzed the outcome of 963 evaluable patients with regards to possible side-effects or complications attributable to pelvic lymph node dissection. They concluded that the complication rate increases virtually in direct proportion to the number of nodes removed. This observation seems logical; however, the following points should be considered:

- They define a removal of ≥ 10 nodes as an extended pelvic lymphadenectomy, whereas the removal of < 10 nodes is called a limited lymph node dissection. Usually, the extent of pelvic lymph node dissection is defined by anatomic templates; removal of the lymph nodes along the external iliac vein and the obturator fossa is generally considered a limited pelvic lymph node dissection. With this template, the yield of lymph nodes from both sides is between 10 and 15 lymph nodes [2,3]. If, in addition, the lymph nodes lateral and medial to the internal iliac vessels up to and around the bifurcation of the common iliac artery are removed, the procedure is considered

an extended pelvic lymph node dissection. The median number of lymph nodes removed is then usually between 20 and 25. As Briganti states, however, “lymph nodes along the internal iliac vessels were also removed in some patients”; therefore, it must be assumed that not necessarily all patients classified as such had indeed an extended pelvic lymph node dissection. This assumption is supported by the operating room times, which did not differ between the patient groups they defined. This fact, together with the limited number of nodes removed, may therefore suggest that the authors’ definition of extended lymph node dissection does not necessarily correspond with the generally accepted definition of an extended pelvic lymph node dissection.

- As expected, the most frequently reported complication was lymphoceles, observed in 10.3% of the patients in whom ≥ 10 lymph nodes were removed compared with 4.6% in patients with < 10 lymph nodes removed. Since the authors define lymphocele as “pelvic drainage in excess of 50 cc/d for more than 7 days”, one must assume that, in most patients, it was rather a prolonged lymphorrhoea. Provided the drains are not withdrawn too early, this drainage, in itself, should not result in a serious complication. Even if symptomatic lymphoceles occur, they are easily managed by ultrasound-guided percutaneous drains such as a Cystofix catheter and should not prolong the hospital stay. With regards to the

different incidences of lymphorrhoea, it must also be understood that patients with ≥ 10 nodes removed had a 3-fold incidence of lymph node metastases. A possible blockage of lymphatic vessels by carcinomatous lymphangiosis is a known factor for prolonged lymphorrhoea [4].

- It may also be possible that the surgeon and not so much the surgical technique used could account for differences in the incidence of complications. Indeed, the mean number of nodes removed by the different surgeons ranged between 10.4 and 17.9. Acute urinary retention and urinary anastomotic leakage occurred significantly or substantially more often in patients in whom a higher number of nodes were removed. This finding is hardly attributable to the pelvic lymph node dissection itself; rather, it would suggest that the cause of these complications were the surgeons whose patients more frequently had lymphorrhoea. A significantly lower blood loss in patients in whom ≥ 10 nodes had been removed again speaks for the importance of the surgeon as a confounding factor. Indeed, nobody would conclude that an extended pelvic lymph node dissection should be performed to reduce blood loss during surgery. Instead of adjusting the multivariate analysis for age, prostate-specific antigen (PSA), or tumour stage, an adjustment for the surgeon, incidence of positive nodes, and length of subcutaneous heparin administered would perhaps have been more helpful.
- One must also not forget that the findings are derived from a retrospective analysis and that the same patient and disease factors that motivated the surgeon to remove more nodes might also be associated with an intrinsically higher risk of surgical complications. Even with proper adjustment of the statistical models as discussed above, the potential confounding factors may not have been totally excluded, and the observed associations may not truly represent *causality* of an extended lymphadenectomy to an increased rate of lymphoceles.
- A prospective assessment not only would allow the randomization of patients to limited versus extended dissection (a process that would eliminate the above-listed potential biases) but would also enable standardization of the grading and collection of information concerning the complications. Standardization of data would allow for an analysis including only defined "severe" complications, possibly excluding the asymptomatic lymphoceles.
- Medical considerations in this type of report are much more relevant than the mere reliance on statistical *p* values, particularly in large studies in which the statistical tests may be too sensitive to

small differences in numeric parameters, such as duration of hospital stay. Even if a prolonged hospital stay would be caused by a more extensive lymph node dissection and not, for example, by the surgeons' preference, one may question if a 1.5 d prolonged hospital stay is truly relevant. But to evaluate this association, the potential harm of failing to detect positive nodes in patients having undergone a limited or no lymphadenectomy should also be documented.

While the cited paper is very stimulating and often raises more questions than it is able to answer, there is no doubt that pelvic lymph node dissection may increase morbidity. It is the surgeon's responsibility to keep morbidity as low as possible. This outcome can be achieved if all the lymphatics draining from the leg are meticulously ligated where they enter the pelvis (lacuna vasorum) and if no clips are used because they may be torn off during the radical prostatectomy. Furthermore, as mentioned by the authors, heparin should be injected exclusively into the arm and must be discontinued as early as possible, especially in patients who present with lymphorrhoea, because heparin prevents the formation of fibrin clots that seal the lymphatic vessels.

Despite these precautions, in our own series 2.6% of patients had a prolonged hospital stay or a rehospitalisation resulting from complications related to the pelvic lymphadenectomy. This rate is low when compared with the potential benefits. An increasing body of evidence indicates that not only is staging improved, but meticulous pelvic lymph node dissection may prolong the recurrence-free, if not even the overall, survival [5-7]. Randomized studies are missing and will probably never be done. However, a substantial number of patients in these series remained free of PSA relapse for 10 or more years, an outcome that would not seem plausible if metastatic lymph nodes had been left in. Thus, a substantial number of patients will not be exposed to PSA terrorism and can be spared the detrimental side-effects of (too) early androgen deprivation.

On the basis of recently published results [8] we recommend a pelvic lymph node dissection in all patients who undergo a radical prostatectomy for prostate cancer with a serum PSA > 10 ng/ml and in patients with a serum PSA < 10 ng/ml whenever the biopsy Gleason score is 7 or higher. While it has recently been shown that the primary lymphatic landing sites of the prostate may proximally reach up to the origin of the inferior mesenteric artery, we feel that the template for pelvic lymph node dissection should be similar to the field recommended in bladder cancer, that is, along the external

iliac vessels and obturator fossa, on either side of the internal iliac vessels, and up along the common iliac artery to where the ureter crosses. By using such a template, 65–70% of all primary lymphatic landing sites, or so-called sentinel nodes, are removed. Further removal of nodes along the median portion of the common iliac arteries, the aortic bifurcation, in the intra-aortocaval and paracaval as well as the para-aortic space would enable the removal of approximately 95% of the primary lymphatic landing sites. [9] We feel, however, that the potential additional benefits of this further extension are too small compared with its possible complications, such as injury to the major vessels or to the hypogastric nerves. Preservation of the autonomic innervation positively impacts on urinary continence after radical prostatectomy; therefore, this process should not be compromised [10,11].

In conclusion, there are good reasons to do a meticulous extended pelvic lymph node dissection up to where the ureters cross the common iliac vessels and particularly along both sides of the internal iliac vessels in patients with a serum PSA > 10 ng/ml or in a prostate cancer with a Gleason score of 7 or higher even if the PSA is < 10 ng/ml. With meticulous surgery, serious complications can be avoided, and minor sequelae of short duration, such as a prolonged lymphorrhoea, should not deter the surgeon from providing patients with the potential benefit of removing lymph nodes harboring micrometastases.

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Rebuttal from Authors re: Urs E. Studer, Laurence Collette. Morbidity from Pelvic Lymphadenectomy in Men Undergoing Radical Prostatectomy. *Eur Urol* 2006;50:887–9.

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The extent of pelvic lymphadenectomy in men with clinically localized prostate cancer represents an area of controversy. The controversy surrounds the extent of lymphadenectomy, although it could be argued that more accurate staging reduces the proportion of false-negative lymph node dissections and is associated with the possibility of offering more timely systemic therapy to those individuals with pathologically proven nodal metastases. An even greater area of controversy surrounds the putative survival benefit from pelvic lymphadenectomy. Unfortunately, as in virtually all areas of prostate cancer, successful accrual to randomized trials addressing these two areas of dispute may represent a daunting task.