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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 Briganti A, Chun FKH, Salonia A, et al. Complications and other surgical outcomes associated with extended pelvic lymphadenectomy in men with localized prostate cancer. Eur Urol 2006;50:1006–13.

## 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.

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Despite the absence of data from randomized designs, the benefits and detriments of more accurate staging need to be carefully examined. This is especially true in the era of persistent stage migration, which results in the treatment of an increasingly higher proportion of men with very favorable prostate cancer characteristics [1]. In our manuscript, we attempt to systematically address the question of lymphadenectomy extent by comparing the complications and other surgical outcomes, such as the duration of the surgery, blood loss, and length of stay, between men subjected to extended and less extensive lymphadenectomies.

On the basis of the consideration that the majority of patients treated with radical prostatectomy (RP) for clinically localized prostate cancer have extremely favorable pathologic characteristics, it is clear that not all of these men require a pelvic lymph node dissection (PLND). Those who are at risk of harboring lymph node invasion (LNI) can be identified with the use of highly accurate risk stratification tools. Briganti et al. [2] developed and internally validated a highly accurate (76%) nomogram capable of risk stratifying the probability of LNI in men subjected to an extended pelvic lymph node dissection (ePLND). Given that ePLNDs are not universally performed, Briganti et al. [3] also devised a risk stratification tool that allows inclusion of contemporary men subjected to various PLND extents. Finally, the same authors [4] demonstrated that only some men at risk of LNI require an ePLND, while others can be accurately staged with removal of nodes localized exclusively in the obturator fossa. A predictive tool capable of identifying those in whom the PLND could be limited to an obturator lymph node dissection was 80% accurate. These three tools most objectively identify individuals at risk of LNI and provide the basis for deciding on the extent of PLND, if a PLND is warranted.

These tools help in stratifying the risk of LNI in patients with localized prostate cancer. However, they do not assess the downsides of more extended PLNDs relative to more limited dissections. Complications associated with ePLNDs and limited PLNDs (lPLNDs) represent one of the main deterrents for performing either an lPLND or an ePLND in all men treated with RP, regardless of LNI risk. The effect of PLND extent on the rate of PLND complications has been studied before. On the basis of data from 189 patients, Stone et al. [5] reported a 35.9% laparoscopic ePLND complication rate versus 2%, when a modified PLND was performed. Clark et al. [6] randomized 123 patients to a unilateral ePLND versus a unilateral lPLND and found that complications, which included lymphoceles, deep

venous thromboses, lower extremity edema, pelvic abscess formation, and ureteral injury, occurred 75% of the time on the side of the ePLND. Taken together, these studies indicated that the PLND extent is a predictor of the rate of PLND complications in prospective as well as in retrospective analyses, regardless of the type of surgical approach, laparoscopic or open.

Our findings allowed us to corroborate these previous reports in a larger series of 963 patients, 767 of whom underwent an ePLND versus 196 who were treated with an lPLND [7]. Our data indicated that ePLND was associated with 19.8% complication rate versus 8.2% (p < 0.001) for lPLND. Of all individual complications, the rate of lymphocele was 2-fold higher in ePLND patients (10.3% vs. 4.6%, p = 0.01). Although the remaining individual complication rates failed to reach clear statistical significance, it is important to notice that their cumulative effect was highly significant. Thus, from a clinical perspective, it is clear that patients subjected to an ePLND will succumb to more adverse outcomes than patients staged with an lPLND, whatever the definitions of these adverse outcomes are. Consequently, it is important to weigh the pros and cons of an ePLND. This decision can be made more objective if the risk of LNI is quantified with one or several risk stratification tools.

PLNDs are associated with complications as well as other surgical outcomes, such as blood loss, surgical time, and length of stay. These endpoints represented additional targets of our analyses, which demonstrated that surgical time did not differ according to PLND extent. Blood loss was on average 195 cc lower in the ePLND group. Finally, the average length of stay was 1.6 d longer for ePLND patients. The interpretation of these results requires caution because two procedures may have contributed to the observed results: The PLND and the RP were performed sequentially, and both procedures might have exerted a cumulative effect on the recorded results. The RP prostatectomy may represent the most important contributor to observed blood loss. PLND may be associated with slow bleeding from small caliber vessels. However, venous or arterial trauma at the time of PLND may occasionally lead to more significant bleeding. Lack of clinically meaningful means and range differences between ePLND and lPLND groups suggests that adverse vascular events did not occur in our series. Consequently, our data indicate that an ePLND does not predispose to significant bleeding versus lPLND. It is also noteworthy that, in our series, an ePLND was not associated with significantly longer surgical times. However, the ranges

indicate that, in the ePLND group, surgical times reached 375 min versus 305 min in the lPLND group. It should be emphasized that these outcomes are representative of a centre of excellence, where lymph node dissection of substantially greater extent is performed [2]. Therefore, longer surgical times might be anticipated if ePLNDs are performed by individuals or in centres with less extensive expertise. Our assessment of the length of stay may be affected by the RP, the extent of PLND, as well as by other variables that might determine the length of hospital stay. These variables may include social considerations, such as distance separating patient's residence from the hospital or availability of help at home. Despite these potential sources of bias or confounding, our data suggest that patients subjected to an ePLND on average remained hospitalized for 1.7 d longer than their counterparts subjected to IPLND. This difference was also noted in the distributions of lengths of stay, which extended up to 40 d for men treated with ePLND versus 20 d for men treated with lPLND. This observation in turn does suggest that there were more reasons for keeping ePLND patients in the hospital than there were for men subjected to IPLND.

We thank Drs Studer and Collette for their comments regarding the above findings. We are reassured that they agree that the extent of PLND does predispose to a higher rate of complications. We are equally reassured that Dr Studer's group have used the same nodal count criterion of 10 nodes to substantiate inclusion in the ePLND group and to limit the variability that may originate from variability in individual patient nodal density, anatomic variability, and in possible nuances related to the dissection limits, despite a standard ePLND template [8]. Drs Studer and Collette question the definition of lymphocele that was used in this report and suggest the use of lymphorrhea instead. It is a fact that the wording used to define lymphoceles in various prostate cancer PLND manuscripts varies substantially [5,6,9]. Although there is no consensus regarding the definition of lymphoceles, a general agreement exists nonetheless that this complication as a group of events with somewhat variable definitions is non-negligible after PLND. To circumvent future problems with nonstandard definitions, consensus definitions for PLND complications could eventually be defined.

Adjusting for intersurgeon variability represents another helpful suggestion made by Drs Studer and Collette. Indeed intersurgeon variability may represent a source of systematic bias and is usually adjusted for in interinstitutional analyses. We recognize that generally speaking the influence of the surgeon on the outcome and morbidity of any surgical procedure per se is extremely important. However, our analysis relies on data from a single institution at which the same technique was used by all surgeons. Thus, we do not believe that adjustment for the effect of surgeon variability could have appreciably changed our results. Moreover, our data do not lose power because each surgeon will weigh these messages depending on his own personal experience. As a matter of fact, this type of adjustment was not made in any previous reports addressing the topics of LNI or PLND complications. To explore ways to clarify this issue, a study assessing, in a prospective fashion, the influence of the surgeon on the morbidity related to both limited and extended lymphadenectomy is currently ongoing.

Drs Studer and Collette also suggest inclusion of other variables, such as length of heparin therapy or number of positive nodes, for further adjustment. Although adjustment for some variables is needed, excessive adjustment should be avoided because models may be overfitted. Moreover, from a practical perspective, it might not be ideal to adjust for prophylaxis directed at preventing some of the ePLND complications because this adjustment may obliterate the association between these complications and the extent of PLND. However, a standard protocol of heparin prophylaxis is used for all patients undergoing RP at our institution [10]. Moreover, if prediction of complications before PLND is of interest, it is not practically advisable to adjust for variables that are not known before the PLND, such as whether lymph nodes will be positive and how many positive nodes will be present. Despite the above differences in opinion, we do agree with Drs Studer and Collette that the design of our study cannot guarantee causality. We demonstrate instead a number of statistically significant associations between the extent of PLND and the complication rate. Indeed, only randomized designs can, not decidedly, but more definitely prove causality. To the best of our knowledge only one randomized design addressed the effect of PLND extent on the rate of complications. In this report Clark et al. [6] support our results, which suggest that PLND extent causes a higher rate of complications. Finally, we agree with Drs Studer and Collette that most papers addressing novel topics report novel facts, but also generate new hypotheses. The field of PLND in men with clinically localized prostate cancer is in active evolution. Consequently, there is an urgent need for testing of new hypotheses, and for more extensive and thorough testing of previously reported findings, which are virtually invariably based on single institution or even single surgeon series. These limitations may undermine the generalizability and the validity of our reports as much as those of other investigators. These problems could be circumvented by a multiinstitutional task force with an unbiased, structured prospective agenda.

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