Should We Perform Imaging-Guided Lymph Node Dissection in Patients with Lymphatic Recurrence of Prostate Cancer after Radical Prostatectomy?

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Nearly 30–40% of patients who undergo radical prostatectomy present with biochemical evidence of cancer recurrence and, after a mean time of 3 yr, 10–30% of them will develop clinical recurrence [1]. The diagnostic work-up in the presence of biochemical relapse should be conducted with a view to distinguishing between the probability of local failure only or of distant failure, and this is essentially guided by the kinetics of the prostate-specific antigen (PSA) values and the initial pathology. Unfortunately, traditional imaging techniques are neither adequately sensitive nor very specific for both the early identification of the local recurrence (which is the sole tumor recurrence amenable to a “curative treatment” with salvage radiotherapy) and the simultaneous exclusion of the distant recurrence. Furthermore, when a local recurrence seems to be excluded and a systemic relapse is presumed, imaging techniques such as bone scan or computed tomography (CT) are of no additional diagnostic value unless the PSA serum level is >20 ng/ml, and generally, these patients undergo “palliative” treatment with hormonal deprivation. At the present time, there is no therapy that can be considered curative for such patients [2].

Thanks to more recent metabolic imaging techniques—in particular $^{11}$C/$^{18}$F-choline and $^{11}$C-acetate positron emission tomography (PET), which combine morphological and functional information—it is now possible to identify the site of recurrence in a single step, earlier, and with better accuracy than with conventional imaging (e.g., better sensitivity and much higher specificity). It has been reported that PET/CT detects 40–70% of prostate cancer recurrences with a sensitivity that increases parallel to increases in PSA values and may be highly accurate even with low (<3–5 ng/ml) PSA levels [3].

As a result of these developments, urologists are now increasingly faced with cases of “isolated” pelvic or retroperitoneal lymph node metastasis (LNM) visualized at PET/CT in patients with biochemical recurrence after radical prostatectomy. Such cases raise a number of interesting questions in daily practice. Should these cases always be considered as systemic disease to be treated with hormonal therapy, or is it also possible to consider surgery as a therapeutic option for these patients? Very recently, Scattoni et al reported their experience with pelvic and retroperitoneal lymph node dissection (LND) in patients with lymph node recurrence detected with $^{11}$C-choline PET/CT after radical prostatectomy or primary radiotherapy, with a mean number of 21.9 nodes removed (range: 4–74) [4]. The authors found a low incidence of complications with quite good oncologic results (about 30% of PSA relapse-free survival with no hormonal therapy after a mean follow-up of 15 mo [P. Rigatti, unpublished data, 2008]). Schilling et al have verified the accuracy of $^{11}$C-choline PET/CT in the diagnosis of lymph node recurrence after radical prostatectomy.
or primary radiotherapy, with a median of 5.5 (range: 1–22) nodes removed [5]. They noted a PSA relapse in all cases after an initial reduction of PSA after a lymphadenectomy, with a mean follow-up of 11 mo.

Does the surgical treatment of LNM have a role for patients with prostate cancer recurrence? Can the surgical approach be considered as curative for some of these patients? If we look at the role of pelvic LND (PLND) during radical prostatectomy, when considering pN0 patients, many authors have reported better results in terms of PSA relapse-free survival and tumor progression for those patients who were treated with a more extended PLND rather than a limited one [6,7]. Furthermore, among patients with LNM after radical prostatectomy, a more extended LND may offer a better cancer-specific survival only for those with low lymph node density (<15–20%) [8,9]. So, even in the absence of a randomized trial to verify this finding, it can be said that PLND in association with radical prostatectomy may cure some prostate cancer patients with LNM but only with a “meticulous” LND and only in cases of a low lymphatic tumor burden.

Is choline or acetate PET/CT adequate for the detection of this kind of metastasis? Is this imaging accurately accurate for cases with a low lymphatic tumor burden? It would seem that this is not yet so. We recently evaluated the accuracy of [11C]choline PET/CT for preoperative lymph node staging of 57 patients with intermediate- and high-risk prostate cancer before radical prostatectomy and noted a poor sensitivity for the detection of the small metastases (detection rate of <20% for tumor deposits of <5 mm) but a very high specificity [10]. Furthermore, [11C]-choline PET/CT detected only 41.4% of the total LNMs, and we concluded that when [11C]-choline PET/CT visualizes a LNM, the tumor burden is probably higher than had been expected.

It appears that the surgical dissection of LNM detected by PET/CT in recurrent prostate cancer after radical prostatectomy can be definitely curative (eg, absence of PSA relapse with no hormonal therapy with long-term follow-up) in only a very small number of these patients, essentially because of the low sensitivity of the current imaging techniques; it goes without saying that more sensitive imaging techniques and new radiotracers for PET are eagerly awaited.

Nevertheless, we think that, even if it cannot be considered definitely curative, this kind of surgical approach does have a role in some selected cases. It may be particularly useful in the context of a multimodal treatment because it can increase the PSA relapse-free survival in some patients.

Furthermore, by diminishing the volume of the target tumor, it can improve the efficacy of the medical treatment. It can also have a positive psychological effect on younger patients, who may prefer this kind of treatment to systemic therapy.

Patients with LNM detected at PET/CT after radical prostatectomy are certainly not a homogeneous population, and we need to ask whether they all underwent radical prostatectomy with concomitant extended PLND, whether they were operated laparoscopically, whether the lymph nodes removed during radical prostatectomy were correctly analyzed by the pathologist, and whether any of the patients had been previously treated with hormonal therapy. Undoubtedly, the assessment of a patient with a metastatic lymph node detected with PET/CT after radical prostatectomy should take all of these variables into account.

Other important aspects need to be considered before recommending this kind of surgery. In patients with biochemical relapse, at which level of serum PSA should we look for LNM with PET/CT? Should we interrupt hormonal treatment before PET/CT? Is there an upper limit (in terms of location and number of positive lymph nodes) for the removal of LNM? Last but not least, is the surgeon adequately skilled to perform this kind of surgery? At the moment, the answers remain controversial, and there may be a need for a multicentric approach with the participation of expert surgeons who “believe” in this kind of surgery.

Conflicts of interest: The authors have nothing to disclose.

References


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