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Contemporary Role of Salvage Lymphadenectomy in Patients with Recurrence Following Radical Prostatectomy

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Abstract

Context: Prostate cancer (PCa) patients with isolated clinical lymph node (LN) relapse, limited to the regional and/or retroperitoneal LNs, may represent a distinct group of patients who have a more favorable outcome than men with progression to the bone or to other visceral organs. Some data indirectly denote a beneficial impact of pelvic LN dissection on survival in these patients.

Objective: To provide an overview of the currently available literature regarding salvage LN dissection (SLND) in PCa patients with clinical relapse limited to LNs after radical prostatectomy (RP).

Evidence acquisition: A systematic literature search was conducted using the Medline, Embase, and Web of Science databases to identify original articles, review articles, and editorials regarding SLND. Articles published between 2000 and 2012 were reviewed and selected with the consensus of all the authors.

Evidence synthesis: Contemporary imaging techniques, such as 11C-choline positron emission tomography and diffusion-weighted magnetic resonance imaging, appear to enhance the accuracy in identifying LN relapse in patients with biochemical recurrence (BCR) and after RP. In these individuals, SLND can be considered as a treatment option. The currently available data suggest that SLND can delay clinical progression and postpone hormonal therapy in almost one-third of the patients, although the majority will have BCR. An accurate and attentive preoperative patient selection may help improve these outcomes. The most frequent complication after SLND was lymphorrhea (15.3%), followed by fever (14.5%) and ileus (11.2%). It is noteworthy that all examined cohorts originated from retrospective single-institution series, with limited sample size and short follow-up. Consequently, the current findings cannot be generalized and warrant further investigation in future prospective trials.

Conclusions: The current data suggest that SLND represents an option in patients with disease relapse limited to the LNs after RP; however, more robust data derived from well-designed clinical trials are needed to validate the role of SLND in this selected patient population.

Patient summary: Salvage lymph node dissection (SLND) represents a treatment option in for patients with prostate cancer relapse limited to the lymph nodes; however, more robust data derived from well-designed clinical trials are needed to validate the role of SLND in this selected patient population.

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1. Introduction

In contemporary surgically treated prostate cancer (PCa) patients, the rate of biochemical recurrence (BCR) after radical prostatectomy (RP) may reach 40% [1–4]. A postoperative increase in prostate-specific antigen (PSA) level is an index of tumor relapse, which could be localized or systemic. Traditionally, salvage radiotherapy is offered to patients with a suspected localized pelvic recurrence, whereas hormonal therapy is offered to those with systemic spread of the disease [5]. However, current advances in clinical imaging techniques have allowed the identification of a new group of patients with a unique relapse pattern. These are patients with “systemic” disease progression, which is limited to the regional and/or retroperitoneal lymph nodes (LNs). These patients will be referred to as patients with *clinical LN relapse*.

Patients with isolated clinical LN relapse may represent a distinct group of patients who have a more favorable outcome compared with men with progression to the bone or to other visceral organs [6]. Recent reports found that some of these patients may benefit from favorable cancer-control outcomes when surgically treated [7,8]. This finding is in line with previous retrospective data showing that extended pelvic LN dissection (ePLND) could offer favorable cancer control outcomes in PCa with LN invasion (LNI) at RP, especially when the LNI volume is low (two or fewer positive nodes) [9,10]. It is interesting to note that the favorable impact of RP and ePLND held true even in patients who did not receive adjuvant hormonal therapy after surgery. Such data indirectly denote a beneficial impact of pelvic LN dissection (PLND) on survival in these individuals. However, it is not possible to directly apply these findings to patients with post-RP clinical LN relapse, because the latter represent a distinct clinical setting. Nevertheless, it may be hypothesized that at least some patients with evidence of limited clinical LN relapse after RP can benefit from salvage LN dissection (SLND).

It is noteworthy that clinical LN relapse can be the direct consequence of a suboptimal PLND at initial treatment. Indeed, during the last two decades, the majority of surgically treated PCa patients received either a limited PLND (only obturator fossa) or no PLND at all during initial treatment [11]. This finding was confirmed in contemporary patients, in whom PLND was omitted in 28.5% and 18.2% of patients with respectively intermediate- and high-risk tumors treated with open RP, and in 49.5% and 32.7% of patients treated with robotic-assisted RP, respectively [12]. These findings imply that even when there are clear clinical indications, PLND is not always performed. It appears that the introduction of laparoscopic and robot-assisted RP has significantly contributed to the increased omission of PLND [12]. This situation may translate to a higher proportion of patients with clinical LN relapse in the coming years, which further points out the necessity of working out an optimal treatment strategy in these individuals. We reviewed the data regarding the currently highly controversial procedure of SLND in patients with clinical LN relapse after RP.

2. Evidence acquisition

We performed a literature search in December 2012 using the Medline, Embase, and Web of Science databases. We identified original articles, review articles, and editorials addressing the role of SLND in PCa. Articles written in any language other than English were excluded. The following limits were used: humans; and gender (male). Keywords included *prostate cancer*, *salvage lymphadenectomy*, *salvage lymph node dissection*, and *salvage lymph node excision*. All titles were screened, and studies were excluded if obviously irrelevant. If there was any doubt concerning the eligibility of a study, abstracts—and if necessary, the full text—were examined. Additional references were identified from the reference lists of these articles (Fig. 1). It is noteworthy that all included articles consisted of case series, which represent level 4 evidence.

To identify publications that address the evolution of imaging techniques and their role in the management of patients with PCa relapse, additional sources were gathered by including the following keywords, arranged in variable combinations: *prostate cancer*, *positron emission tomography (PET)*, *computed tomography (CT)*, *choline*, *magnetic resonance imaging (MRI)*, *diffusion-weighted MRI*, *PSA*, *biochemical relapse*, *restaging*, and *recurrence*.

3. Evidence synthesis

3.1. Diagnosis and staging of lymph node relapse after radical prostatectomy

Cross-sectional imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), have shown poor ability to detect LN metastasis in patients with PCa [13] because a volumetric measure (ie, LN diameter) was traditionally used to define LNI status. This drawback limited the use of these imaging techniques in the preoperative staging work-up. However, in recent years, several developments and improvements were introduced to the traditional imaging techniques that escalated their performance as LN staging procedures. In the current review, we focused on two relatively novel imaging techniques that are increasingly recognized as promising staging tools for clinical LN relapse.

3.1.1. 11C-Choline positron emission tomography/computed tomography scan

The theory beyond the use of the 11C-choline positron emission tomography (PET)/CT scan is that tumor cells have a higher turnover of essential cell membrane components, such as phosphatidylcholine. After uptake by tumor cells, radioactive choline is phosphorylated in high concentration and built into the cell membrane, which allows its detection by the PET scan. Since the introduction of 11C-choline PET/CT, several reports have tried to evaluate its role as a staging procedure in PCa patients with BCR after initial radical treatment with curative intent [14–26]. These reports showed a sensitivity that ranged between 38% and 98%. This

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