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Robotic salvage lymph node dissection for nodal-only recurrences after radical prostatectomy: Perioperative and early oncological outcomes

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ABSTRACT

Background: Salvage lymph node dissection (sLND) – performed open or minimally-invasive - is a treatment modality that can be offered to patients with nodal recurrence after radical prostatectomy (RP), especially in times where modern imaging methods like choline- or PSMA-PET/CT are available. Yet, there are only very limited data on the safety and oncological effectiveness of robotic sLND.

Methods: We retrospectively identified patients who underwent robotic sLND at our institution between 2013 and 2017 for nodal recurrence after RP, which had been diagnosed either by ^{18}F-choline- or ^{68}Ga-PSMA-PET/CT. We analyzed perioperative data and early oncological outcomes with a focus on the comparison of patients with preoperative choline- vs. those with preoperative PSMA-PET/CT.

Results: We identified 36 patients who underwent robotic sLND at a median time of 45.3 months [range 3.1;228.6] after RP, with nodal recurrences detected in 25 patients by PSMA- and in 11 by choline-PET/CT. Median preoperative PSA, operation time and blood loss were 1.98 ng/ml [range 0.09;35.15], 129.5 min [range 65;202] and 50 ml [range 0;400], respectively. No high-grade complications occurred. A median number of 6.5 [range 1;25] lymph nodes were removed with a median of 1 [range 0;9] tumor-occupied node. None of the patients received any adjuvant treatment. Median postoperative PSA-change was −57% [range −100; +58] in the PSMA- and +10% [range −91; +95] in the choline-group ($p = 0.015$). 44% of patients in the PSMA- and 18% of patients in the choline-group experienced complete biochemical response (cBCR; PSA <0.2 ng/ml). Median time from sLND to the initiation of further therapy was 12 months [range 2;21.5] in the PSMA-group and 4.7 months [range 2.2;18.9] in the choline-group ($p = 0.001$).

Conclusions: This is the hitherto largest series on robotic sLND for nodal recurrence after RP. Robotic sLND is a feasible therapeutic option with low morbidity, which can at least delay the initiation of further therapy – in some patients up to several years. However, the extend of sLND has to be standardized and randomized trials are needed to finally define the oncological effectiveness of this approach.

1. Introduction

Despite advances in patient-selection and surgical techniques, up to 50% of patients undergoing radical prostatectomy (RP) for organ-confined prostate cancer (PCa) develop biochemical recurrence (BCR) within the first ten years [1,2]. For those, either salvage radiotherapy (sEBRT) to the prostatic bed ± regional lymph nodes or androgen deprivation therapy (ADT) is recommended [3]. In recent years - especially due to the advent of new imaging modalities with high-sensitivity in the setting of BCR after RP [4,5] -

Abbreviations: ADT, androgen deprivation therapy; BCR, biochemical recurrence; cBCR, complete biochemical response; CSS, cancer specific survival; EBRT, extracorporeal beam radiation therapy; IQR, interquartile range; OS, overall survival; PCa, prostate cancer; PET/CT, positron emission tomography/ computed tomography; PSA, prostate specific antigen; PSMA, prostate specific membrane antigen; RP, radical prostatectomy; sLND, salvage lymph node dissection.

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targeted radiotherapy or salvage lymph node dissection (sLND) have been proposed as alternative treatments for patients presenting with solitary or oligo-metastases. Several retrospective studies on the safety and effectiveness of sLND in patients with lymph node recurrence detected by PET/CT are available, summarized in two systematic reviews [6,7]. However, the majority of these studies display major drawbacks limiting their informative value for contemporary patient management: First, in almost all studies choline-PET/CT was used for preoperative imaging, which has been completely replaced by PSMA-PET/CT in clinical practice in the meantime due to higher sensitivity and specificity [8–11]. Second, an evaluation of the oncological effectiveness of sLND is severely restricted by the fact that a substantial proportion of patients received simultaneous or adjuvant ADT or EBRT, thereby diluting the effect of sLND on postoperative PSA-course and oncological end points. Third, there are only very few studies reporting on long-term oncological outcomes of sLND [12,13] and those who do not have an adequately matched control group which received immediate sEBRT or ADT instead of a sLND. Fourth, in most studies an open surgical approach was performed, which might be associated with higher perioperative morbidity compared to minimally-invasive approaches. To date, only three retrospective case series on laparoscopic robot-assisted sLND including 16, 10 and 35 patients have been published [14–16].

In this study, we describe the perioperative and early oncological outcomes of patients who underwent robotic sLND at our institution. With 36 patients, this cohort represents the largest series of robotic sLND published to date. Importantly and in contrast to the aforementioned series, most patients were preoperatively evaluated by PSMA-PET/CT and no adjuvant treatment in terms of ADT or EBRT was performed additionally to sLND.

2. Materials and methods

2.1. Study population

We retrospectively identified patients who underwent robotic sLND at our institution from 2013 to 2017. All patients presented with BCR (two consecutive PSA-rises > 0.2 ng/ml) following RP and underwent ^{18}F-choline-PET/CT (11 patients, “choline-group”) or ^{68}Ga-PSMA-PET/CT (25 patients, “PSMA-group”) to detect recurrences. The selection of patients for choline- or PSMA-PET/CT was purely triggered by the date they presented to our department with choline-PET/CTs used until 2014 and PSMA-PET/CT from 2015 on. Patients were informed about the experimental status of this treatment approach and were planned for robotic sLND by one of five experienced robotic surgeons (CHO, MJ, MSa, MSt, StS). Institutional review board approval for the retrospective analysis of patient data was obtained and the consent of patients to the use of their data was reassured during telephonic interviews.

2.2. Imaging

PET/CT examinations were performed according to standard protocols using ^{68}Ga-labelled PSMA ligands (PSMA-11 = PSMA-HBED-CC) or ^{18}F-labelled Fluormethylcholin (FCH). Briefly, after application of the radionuclide and 500–1000 ml 2% oral iodine contrast agent, a topogram and low-dose CT for attenuation correction were acquired. PET-acquisition was performed 60 (PSMA) or 90 (choline) minutes after injection of the tracer. 10 min before the start of image acquisition, iodine contrast agent was administered intravenously to contrast the ureter and bladder. After PET-acquisition, digital reconstructions in planar view from 36 projections (maximum intensity projections; MIP) and semi-quantitative, region-based analyses (standardized uptake value (SUV) measurement in 5 mm planes) were performed.

2.3. Surgical technique

A six-port transperitoneal approach with a four arm Da Vinci Si system (Intuitive Surgical, Sunnyvale, CA, USA) was used. Port placement was started with a supraumbilical Hasson mini-laparotomy [17] for the camera trocar (12 mm). Thereafter, two 8 mm robotic trocars were placed, each 8 cm lateral to the umbilicus. For extension of sLND up to the aortic bifurcation, these two trocars were placed 2–3 cm more cranial. Further trocars included a 12 mm assistant trocar 2 cm cranial to the right anterior superior iliac spine and a further 8 mm robotic trocar 2 cm cranial to the left anterior superior iliac spine. Another 5 mm assistant trocar was placed between the camera and the right robotic port. Patients were then placed in a steep Trendelenburg position, the robot was docked and intraabdominal pressure was kept at 8–10 mmHg during the whole procedure. The dissection template was defined individually for each patient by the surgeon performing the procedure taking into consideration clinical data and preoperative imaging results. In some patients, only the PET-positive nodes were removed (“targeted dissection”) while in others extended dissection of the pelvic lymph nodes (internal, external and common iliac; obturatory) on one or both sides (“unilateral extended” and “bilateral extended”, respectively) were performed. Besides that, some patients received extended bilateral dissection of the pelvic lymph nodes plus a dissection of retroperitoneal lymph nodes (paraaortic, paracaval, interaortacaval) (“bilateral extended + retroperitoneal”). No wound drainage was routinely placed. No adjuvant EBRT or ADT was given additionally to sLND.

2.4. Perioperative and oncological follow-up data

For all patients, baseline and perioperative characteristics were retrieved from their records. Clinical follow-up data were obtained from the patients' local urologists or by patient interview. Perioperative complications were graded according to the Clavien-Dindo classification [18]. Usually, the first postoperative PSA-level was measured 8–12 weeks after sLND and every 3–6 months thereafter. For the evaluation of early oncological outcomes, the time of follow-up, the rate of patients experiencing complete biochemical response (cBCR), the relative PSA-change after sLND and the time to the initiation of further therapy was analyzed. cBCR was defined as a postoperative PSA-nadir <0.2 ng/ml in concordance with other studies on sLND in PCa [6,7]. Initiation of further therapy upon clinical or biochemical recurrence after sLND was prompted by the patients' treating local urologists on an individual basis.

2.5. Statistics

For continuous variables medians, interquartile ranges (IQR) and ranges are reported. For categorical variables frequencies and proportions are reported. To test for intergroup differences (PSMA- vs. choline-group), Chi-square or Fisher's exact test were used for categorical and Mann-Whitney *U* Test for continuous variables. Survival curve analysis (time to further therapy) was performed using the Kaplan-Meier-Method and the log-rank test. To calculate these statistics, SPSS Statistics Version 23 was used (IBM, Armonk, NY, USA).

3. Results

3.1. Baseline patient characteristics and preoperative data

We identified 36 patients with a median age of 66 years [range