EUROPEAN UROLOGY ONCOLOGY xxx (xxxx) xxx–xxx

available at www.sciencedirect.com
journal homepage: euoncology.europeanurology.com

European Association of Urology

# Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study

*Pawel Rajwa*[a,b], *Daniele Robesti*[c,d], *Michael Chaloupka*[e], *Fabio Zattoni*[f], *Alexander Giesen*[g], *Nicolai A. Huebner*[a], *Aleksandra Krzywon*[h], *Marcin Miszczyk*[i], *Matthias Moll*[j], *Rafał Stando*[k], *Edoardo Cisero*[l], *Sofiya Semko*[m], *Enrico Checcucci*[n], *Gaëtan Devos*[g], *Maria Apfelbeck*[e], *Cecilia Gatti*[n], *Giancarlo Marra*[o], *Roderick C.N. van den Bergh*[p], *Gregor Goldner*[j], *Sazan Rasul*[q], *Francesco Ceci*[r], *Fabrizio Dal Moro*[f], *Francesco Porpiglia*[l], *Paolo Gontero*[o], *Anders Bjartell*[s], *Christian Stief*[e], *Axel Heidenreich*[m], *Steven Joniau*[g], *Alberto Briganti*[c,d], *Shahrokh F. Shariat*[a,t,u,v,w,x,*], *Giorgio Gandaglia*[c,d], *on behalf of the EAU-Young Academic Urologists (YAU) Prostate Cancer Working Party*

[a] *Department of Urology, Medical University of Vienna, Vienna, Austria;* [b] *Department of Urology, Medical University of Silesia, Zabrze, Poland;* [c] *Unit of Urology/Division of Oncology, Gianfranco Soldera Prostate Cancer Lab, IRCCS San Raffaele Scientific Institute, Milan, Italy;* [d] *Vita-Salute San Raffaele University, Milan, Italy;* [e] *Department of Urology, LMU Klinikum, Ludwig-Maximilians University Munich, Munich, Germany;* [f] *Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy;* [g] *Department of Urology, University Hospitals Leuven, Leuven, Belgium;* [h] *Department of Biostatistics and Bioinformatics, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Gliwice, Poland;* [i] *IIIrd Department of Radiotherapy and Chemotherapy, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice, Poland;* [j] *Department of Radiation Oncology, Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria;* [k] *Department of Radiotherapy, Holy Cross Cancer Center, Kielce, Poland;* [l] *Division of Urology, Department of Oncology, School of Medicine, University of Turin, San Luigi Hospital, Orbassano, Italy;* [m] *Department of Urology, Faculty of Medicine, University Hospital Cologne, University Cologne, Cologne, Germany;* [n] *Department of Surgery, Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Turin, Italy;* [o] *Department of Urology, Città della Salute e della Scienza, University of Turin, Turin, Italy;* [p] *Department of Urology, St Antonius Hospital, Utrecht, The Netherlands;* [q] *Department of Biomedical Imaging and Image-Guided Therapy, Medical University of Vienna, Vienna, Austria;* [r] *Division of Nuclear Medicine, IEO European Institute of Oncology, IRCCS, Milan, Italy;* [s] *Department of Urology, Skåne University Hospital, Lund University, Malmö, Sweden;* [t] *Karl Landsteiner Institute of Urology and Andrology, Vienna, Austria;* [u] *Department of Urology, Second Faculty of Medicine, Charles University, Prague, Czech Republic;* [v] *Division of Urology, Hourani Center for Applied Scientific Research, Al-Ahliyya Amman University, Amman, Jordan;* [w] *Department of Urology, Weill Cornell Medical College, New York, NY, USA;* [x] *Department of Urology, University of Texas Southwestern, Dallas, TX, USA*

**Article info**

***Article history:***
Received 18 June 2023
Received in Revised form
29 August 2023
Accepted 11 September 2023

**Abstract**

***Background:*** De novo oligometastatic prostate cancer (omPCa) on prostate-specific membrane antigen (PSMA) positron emission tomography (PET) is a new disease entity and its optimal management remains unknown.

***Objective:*** To analyze the outcomes of patients treated with cytoreductive radical prostatectomy (cRP) for omPCa on PSMA-PET.

***Design, setting, and participants:*** Overall, 116 patients treated with cRP at 13 European centers were identified. Oligometastatic PCa was defined as miM1a and/or miM1b with

* Corresponding author. Department of Urology, Comprehensive Cancer Center, Medical University Vienna, Vienna General Hospital, Währinger Gürtel 18-20, A-1090 Vienna, Austria. Tel. +43 1 40400 26150; Fax: +43 1 40400 23320.
E-mail address: shahrokh.shariat@meduniwien.ac.at (S.F. Shariat).

https://doi.org/10.1016/j.euo.2023.09.006


Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

**Associate Editor:**
Jeremy Teoh

***Keywords:***
Prostate cancer
Oligometastatic
Prostate-specific membrane antigen positron emission tomography
Cytoreductive radical prostatectomy
Multimodal therapy

five or fewer osseous metastases and/or miM1c with three or fewer lung lesions on PSMA-PET.

***Intervention:*** Cytoreductive radical prostatectomy.

***Outcome measurements and statistical analysis:*** Thirty-day complications according to Clavien-Dindo, continence rates, time to castration-resistant PCa (CRPC), and overall survival (OS) were analyzed.

***Results and limitations:*** Overall, 95 (82%) patients had miM1b, 18 (16%) miM1a, and three (2.6%) miM1c omPCa. The median prebiopsy prostate-specific antigen was 14 ng/ml, and 102 (88%) men had biopsy grade group ≥3 PCa. The median number of metastases on PSMA-PET was 2; 38 (33%), 29 (25%), and 49 (42%) patients had one, two, and three or more distant positive lesions. A total of 70 (60%) men received neoadjuvant systemic therapy, and 37 (32%) underwent metastasis-directed therapy. Any and Clavien-Dindo grade ≥3 complications occurred in 36 (31%) and six (5%) patients, respectively. At a median follow-up of 27 mo, 19 (16%) patients developed CRPC and eight (7%) patients died. The 1-yr urinary continence rate was 82%. The 2-yr CRPC-free survival and OS were 85.8% (95% confidence interval [CI] 78.5–93.7%) and 98.9% (95% CI 96.8–100%), respectively. The limitations include retrospective design and short-term follow-up.

***Conclusions:*** Cytoreductive radical prostatectomy is a safe and feasible treatment option in patients with de novo omPCa on PSMA-PET. Despite overall favorable oncologic outcomes, some of these patients have a non-negligible risk of early progression and thus should be considered for multimodal therapy.

***Patient summary:*** We found that patients treated at expert centers with surgery for prostate cancer, with a limited number of metastases detected using novel molecular imaging, have favorable short-term survival, functional results, and acceptable rates of complications.



## 1. Introduction

Prostate-specific membrane antigen (PSMA) positron emission tomography (PET) has been proposed to stage newly diagnosed prostate cancer (PCa) patients with intermediate- or high-risk disease [1,2], thanks to its superior sensitivity and specificity compared with conventional imaging, namely, computed tomography (CT) and bone scan [2]. The widespread use of PSMA-PET has, thereby, led to a stage migration with a more common diagnosis of metastatic disease (in up to one out of five patients), changing management in one out of three patients [2,3]. The number of patients diagnosed with oligometastatic PCa (omPCa) has increased sharply, with approximately 50% of patients with metastatic PCa detected using PSMA-PET to have omPCa, a distinct clinical entity with expected better prognosis than metastatic PCa based on conventional imaging [4,5]. The role of local therapies, including cytoreductive radical prostatectomy (cRP), has been proposed in this setting to delay progression by local tumor debulking and improve survival [6,7]. This, together, in the context of multimodal approaches that include systemic and metastasis-directed (MDT) therapies, could ultimately improve oncologic outcomes [8–11]. Previous studies demonstrated that cRP is a safe and feasible therapy associated with favorable medium-term outcomes in well-selected patients diagnosed with omPCa [12–14]. However, available evidence supporting cRP in omPCa is derived from patients diagnosed using conventional imaging and, therefore, might not be generalizable to men preoperatively staged with PSMA-PET [15]. Information on the safety and short-term effectiveness of cRP for omPCa on PSMA-PET is key to guiding clinicians and delivering the optimal therapy in this novel disease stage. To overcome this lack of knowledge, we conducted a multicenter study of omPCa treated with cRP. Our primary aims were to analyze the safety and short- to mid-term oncologic outcomes of patients who underwent cRP for de novo omPCa diagnosed using PSMA-PET imaging. The secondary goal was to evaluate functional results and factors associated with favorable outcomes.

## 2. Patients and methods

### 2.1. Study population

Under institutional review boards' approvals at participating centers, we retrospectively identified patients within the maintained cohorts from 13 referral centers in Europe (Austria, Belgium, Germany, Poland, and Italy). We included individuals treated with cRP for de novo omPCa on PSMA-PET between 2014 and 2022. Oligometastatic PCa was defined as miM1a and/or miM1b with five or fewer osseous metastases and/or miM1c with three or fewer lung lesions, with or without miN positivity [6,14]. Our broader definition of omPCa, compared with those reported previously [6,14], has been implemented due to the higher accuracy of PSMA-PET than conventional imaging and the potential indolent natural history of patients with PCa lung metastases [16]. Patients who received neoadjuvant systemic therapy before baseline PSMA-PET imaging were excluded

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

**Table 1 – Baseline characteristics, prostate MRI, and biopsy variables of 116 patients undergoing cRP for omPCa diagnosed using PSMA-PET imaging**

| Characteristic | *N* = 116 [a] |
|---|---|
| *Baseline characteristics* | |
| BMI | 26 (24, 30) |
| ECOG status | |
| 0 | 88 (76) |
| 1 | 23 (20) |
| 2 | 4 (3.4) |
| 3 | 1 (0.9) |
| DRE | |
| cT1c | 20 (17) |
| cT2 | 68 (59) |
| cT3–4 | 28 (24) |
| Age at diagnosis (yr) | 66 (60, 72) |
| Baseline PSA (ng/ml) | 14 (7, 46) |
| Germline testing performed | |
| No | 102 (88) |
| Yes | 14 (12) |
| DDR mutations on germline testing | |
| No | 11 (79) |
| Yes | 3 (21) |
| *Prostate MRI and biopsy* | |
| Prebiopsy prostate MRI performed | |
| No | 46 (40) |
| Yes | 70 (60) |
| Highest PI-RADS score on prostate MRI | |
| 3 | 2 (2.9) |
| 4 | 13 (19) |
| 5 | 54 (77) |
| No ROI | 1 (1.4) |
| Dominant lesion diameter on prostate MRI (mm) | 20 (15, 26) |
| ECE on prostate MRI [b] | |
| No | 26 (38) |
| Yes | 42 (62) |
| SVI on prostate MRI [b] | |
| No | 42 (62) |
| Yes | 26 (38) |
| Rectum/bladder infiltration on prostate MRI [b] | |
| No | 63 (93) |
| Yes | 5 (7) |
| Prostate volume (ml) | 40 (32, 56) |
| Biopsy ISUP GG | |
| 1 | 6 (5.2) |
| 2 | 8 (6.9) |
| 3 | 14 (12) |
| 4 | 48 (41) |
| 5 | 40 (34) |

BMI = body mass index; cRP = cytoreductive radical prostatectomy; DDR = DNA damage response and repair; DRE = digital rectal examination; ECE = extracapsular extension; ECOG = Eastern Cooperative Oncology Group; IQR = interquartile range; ISUP GG = International Society of Urological Pathology Gleason grade; MRI = magnetic resonance imaging; omPCa = oligometastatic prostate cancer; PET = positron emission tomography; PI-RADS = Prostate Imaging Reporting and Data System; PSA = prostate-specific antigen; PSMA = prostate-specific membrane antigen; ROI = region of interest; SVI = seminal vesicle invasion.

[a] Median (IQR); *n* (%).

[b] Detailed prostate MRI staging data were missing for two (2.8%) patients.

**Table 2 – Staging imaging data of 116 patients treated with cRP for omPCa diagnosed using PSMA-PET imaging**

| Characteristic | *N* = 116 [a] |
|---|---|
| **Staging imaging** | |
| *Baseline PSMA-PET imaging* | |
| Baseline PSMA-PET | |
| PSMA-PET/CT | 102 (88) |
| PSMA-PET/MRI | 14 (12) |
| Tracer | |
| 18F | 36 (31) |
| 68Ga | 80 (69) |
| miT stage | |
| miT1 | 1 (0.9) |
| miT2 | 63 (54) |
| miT3 | 39 (34) |
| miT4 | 13 (11) |
| miN stage | |
| miN0 | 51 (44) |
| miN1 | 65 (56) |
| Number of PLNs on PSMA-PET | 1 (0, 4) |
| miM stage | |
| miM1a | 18 (16) |
| miM1b | 95 (82) |
| miM1c | 3 (2.6) |
| Certainty of miM+ lesions | |
| Equivocal | 24 (21) |
| Certain | 92 (79) |
| Number of miM1a metastasis | 0 (0, 2) |
| | Range: 1–21 |
| Among patients with miM1a metastasis | 3 (2, 5) |
| No miM1a metastasis | 72 (62) |
| Number of miM1b metastasis | 1 (1, 2) |
| | Range: 1–5 |
| Among patients with miM1b metastasis | 2 (1, 3) |
| No miM1b metastasis | 18 (16) |
| Number of miM1c metastasis | Range: 1–3 |
| No miM1c | 113 (97) |
| Total number of distant metastasis | 2 (1, 4) |
| | Range: 1–21 |
| Second PSMA following neoadjuvant therapy before cRP | |
| No | 83 (72) |
| Yes | 33 (28) |
| *Conventional imaging* | |
| Conventional imaging performed | |
| No | 37 (32) |
| Yes | 79 (68) |
| cN stage [b] | |
| cN0 | 47 (69) |
| cN1 | 21 (31) |
| cM stage | |
| cM0 | 33 (42) |
| cM1a | 14 (18) |
| cM1b | 32 (41) |

18F = fluorine-18; 68Ga = gallium-68; cRP = cytoreductive radical prostatectomy; CT = computed tomography; IQR = interquartile range; MRI = magnetic resonance imaging; omPCa = oligometastatic prostate cancer; PET = positron emission tomography; PLN = pelvic lymph node dissection; PSMA = prostate-specific membrane antigen.

[a] Median (IQR); *n* (%).

[b] cN stage was missing for 11 (14%) patients; only bone scan was performed.

from the analysis. We have included patients regardless of conventional imaging data.

### 2.2. Procedures

#### 2.2.1. PSMA-PET imaging

All PSMA-PET scans were carried out at high-volume centers as per local protocols. For anatomical correlation, PET images were taken from the skull base to the upper thighs and paired with a CT scan or magnetic resonance imaging (MRI). The attenuation was corrected using CT or MRI images; all PSMA-PET images were performed according to European Association of Nuclear Medicine (EANM) guidelines [17]. At referral facilities, experienced nuclear medicine physicians analyzed PSMA-PET scans. Except for locations where the uptake is physiologically elevated, lesions with tracer uptake equal to or higher than the liver were considered positive. The presence and number of distant and pelvic lymph node metastases were reported. Using the anatomy from a CT scan or MRI, the anatomical site was identified. MRI performed before biopsy or cRP

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

**Table 3 – Treatment details and outcomes in 116 patients undergoing cRP for omPCa diagnosed using PSMA-PET**

| Characteristic | *N* = 116 [a] |
|---|---|
| *cRP* | |
| cRP approach | |
| Open | 50 (43) |
| Laparoscopic | 2 (1.7) |
| Robot assisted | 64 (55) |
| PLND | |
| No | 6 (5.2) |
| Yes | 110 (95) |
| Yes, extended | 72 (62) |
| pT | |
| pT2 | 19 (16) |
| pT3a | 27 (23) |
| pT3b | 65 (56) |
| pT4 | 2 (1.7) |
| Complete pathological response (pT0) | 3 (2.6) |
| pN | |
| pN0 | 59 (51) |
| pN1 | 51 (44) |
| pNx | 6 (5.2) |
| Number of collected lymph nodes | 18 (10, 25)<br>Range: 1–136 |
| Number of positive lymph nodes | 1 (0, 3)<br>Range: 0–79 |
| Among patients with positive lymph nodes | 3 (2, 4) |
| cRP GG [b] | |
| 2 | 12 (10) |
| 3 | 12 (10) |
| 4 | 20 (17) |
| 5 | 52 (45) |
| GG could not be assessed due to the impact of systemic therapy | 19 (17) |
| PSM | |
| No | 59 (51) |
| Yes | 57 (49) |
| LVI | |
| No | 71 (61) |
| Yes | 45 (39) |
| OR time (min) | 175 (120, 220) |
| EBL (ml) | 250 (150, 385) |
| Complications | |
| No | 80 (69) |
| Yes | 36 (31) |
| Complications by Clavien-Dindo | |
| No complications | 80 (69) |
| 1 | 23 (20) |
| 2 | 7 (6) |
| 3 | 6 (5) |
| Reoperation | |
| No | 110 (95) |
| Yes | 6 (5.2) |
| Hospital stay (d) | 7 (4, 10) |
| *Multimodal therapy* | |
| Neoadjuvant systemic therapy | |
| No | 46 (40) |
| Yes | 70 (60) |
| ADT alone | 45 (39) |
| ADT plus docetaxel | 7 (6) |
| ADT plus ARSI | 18 (16) |
| Neoadjuvant therapy duration before cRP (mo) | 4 (1, 7) |
| Metastasis-directed therapy | |
| No | 79 (68) |
| Yes | 37 (32) |
| Adjuvant/salvage RT after cRP | |
| No | 73 (63) |
| Yes | 43 (37) |
| *Functional and oncologic outcomes* | |
| Continence at the last follow-up [c] | |
| No | 24 (23) |
| Yes | 82 (77) |
| First PSA value after cRP (ng/ml) | 0.1 (0.0, 0.5) |
| PSA nadir after cRP (ng/ml) | 0.01 (0.01, 0.11) |
| Radiographic progression | |
| No | 96 (83) |
| Yes | 20 (17) |
| CRPC diagnosis | |
| No | 97 (84) |
| Yes | 19 (16) |
| Death | |
| No | 108 (93) |
| Yes | 8 (6.9) |
| Follow-up (mo) | 27 (16, 39) |

ADT = androgen deprivation therapy; ARSI = androgen receptor signaling inhibitors; cRP = cytoreductive radical prostatectomy; CRPC = castration-resistant prostate cancer; EBL = estimated blood loss; GG = Gleason grade; IQR = interquartile range; LVI = lymphovascular invasion; omPCa = oligometastatic prostate cancer; OR = operating room; PCa = prostate cancer; PET = positron emission tomography; PLND = pelvic lymph node dissection; PSA = prostate-specific antigen; PSM = positive surgical margin; PSMA = prostate-specific membrane antigen; RT = radiation therapy.

[a] Median (IQR); *n* (%).

[b] One (0.8%) patient was missing cRP GG data.

[c] Data were available for 106 (91%) patients.

was evaluated and reported using the Prostate Imaging Reporting and Data System (PI-RADS) version 2 [18].

#### 2.2.2. *Cytoreductive radical prostatectomy*

Robot-assisted, laparoscopic, or open cRP with pelvic lymph node dissection (PLND) was performed by board-certified high-volume experienced urologists. At referral centers, experienced uropathologists examined every specimen. Overall, the extent of cRP, systemic therapy administration, and implementation of MDT varied depending on the appraisal of each treating physician at referral centers.

### 2.3. *Endpoints*

Our coprimary endpoints were survival outcomes including castration-resistant PCa (CRPC)-free survival (CRPC-FS), overall survival (OS), and radiographic progression-free survival (rPFS), as well as 30-d complications. CRPC-FS was regarded as the time (in months) from PCa diagnosis to the time of CRPC or death. CPRC diagnosis was made based on European Association of Urology criteria, specifically testosterone <50 ng/dl, biochemical progression (prostate-specific antigen [PSA] >2 ng/ml and three PSA rises, two 50% increases over the nadir), or imaging progression (more than two new bone lesions or a new soft tissue lesion) [19]. OS was defined as the time (in months) from PCa diagnosis to the time of death. We have also evaluated rPFS defined as the time (in months) from PCa diagnosis to any imaging progression (new lesion or increase in lesion size) on any post-cRP subsequent imaging or death. Complications were standardized using Clavien-Dindo classification [20,21]. The secondary study endpoint included functional results considered as continence rate (continent: zero to one pad per 24 h [22]).

### 2.4. *Statistical analysis*

Continuous data were presented as median (interquartile ranges [IQRs]). OS, rPFS, and CRPC-FS were estimated using

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

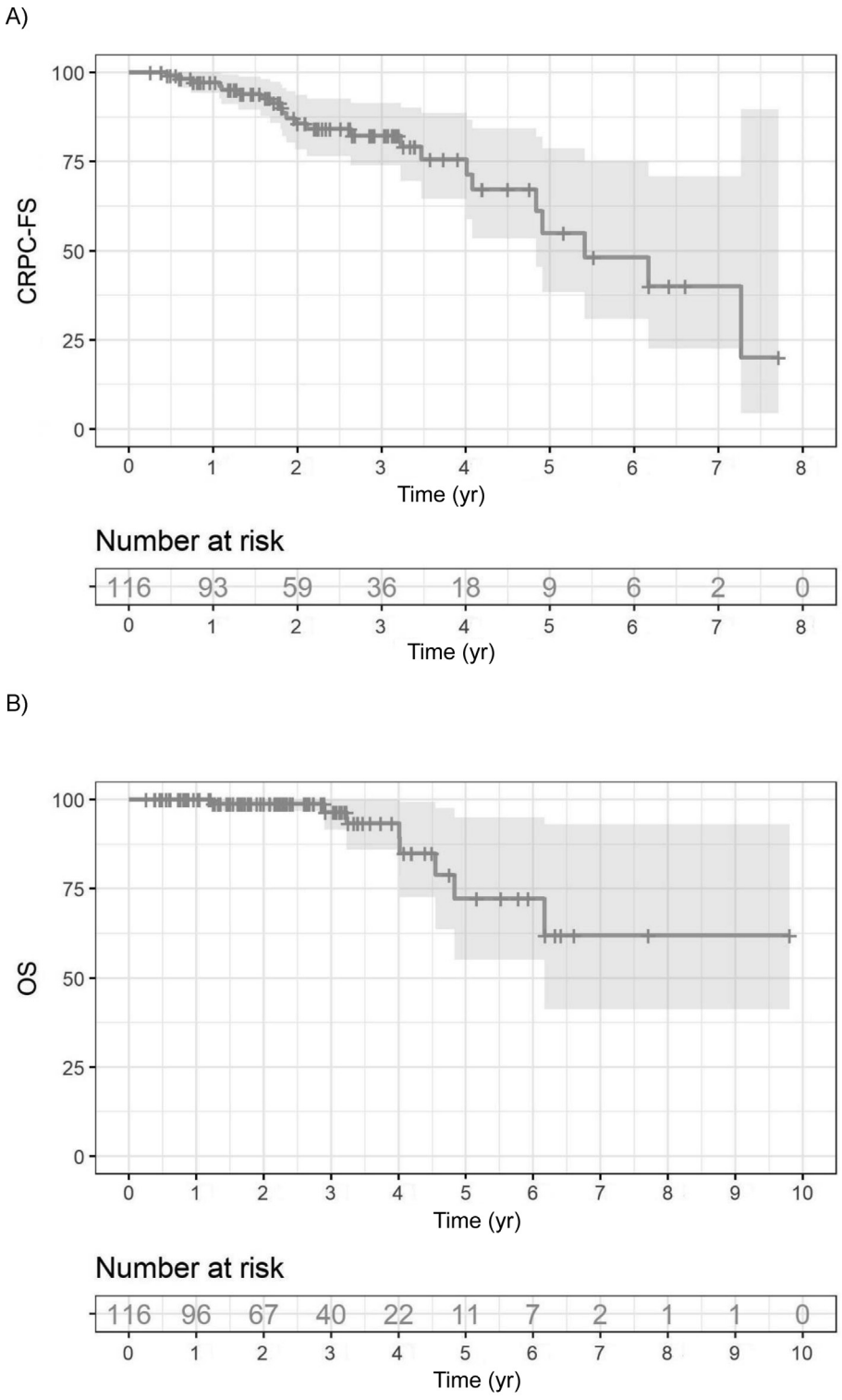


**Fig. 1 – Survival of patients treated with cRP for omPCa diagnosed using PSMA-PET: (A) CRPC-FS, (B) OS, and (C) rPFS. cRP = cytoreductive radical prostatectomy; CRPC-FS = castration-resistant prostate cancer–free survival; omPCa = oligometastatic prostate cancer; OS = overall survival; PET = positron emission tomography; PSMA = prostate-specific membrane antigen; rPFS = radiographic progression-free survival.**

the Kaplan-Meier method. The 95% confidence intervals (CIs) for the survival curves were calculated. The log-rank test was used to compare the survival curves of two or more groups. Hazard ratios (HRs) with 95% CIs were estimated by univariate Cox's proportional hazard regression models. Univariate Cox's proportional hazard regression models were used for investigating the effect of variables on CRPC-FS and rPFS. HRs (95% CIs) for categorical variables were measured when the following criteria were met: at least ten observations (patients) and at least five events per subgroup [23]. All tests were two sided. All computational analyses were performed in the R environment for

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

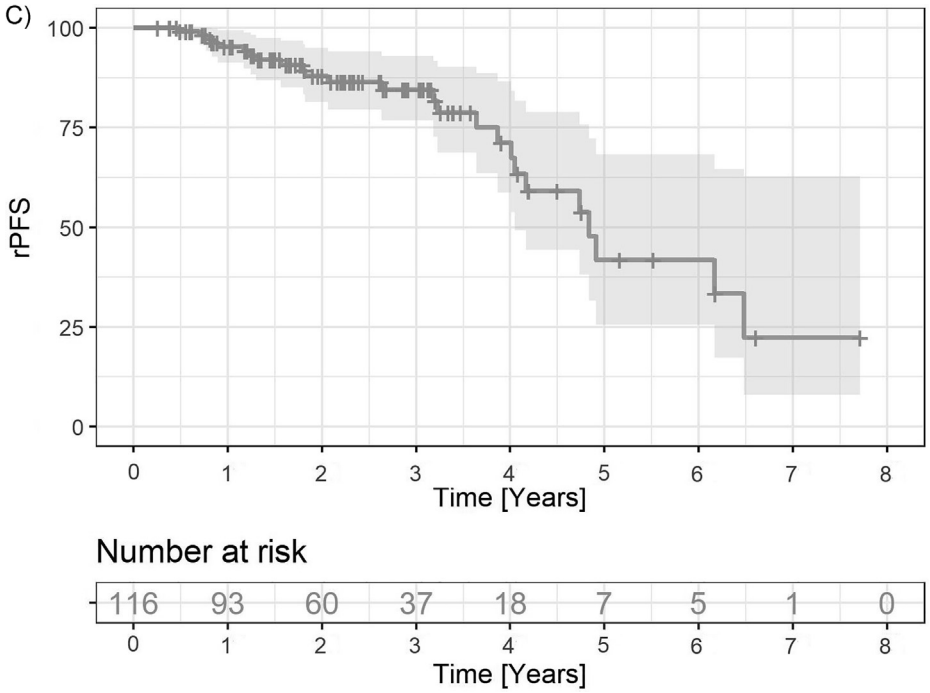


**Fig. 1** (*continued*)

statistical computing, version 4.0.1 (R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org). A $p$ value of <0.05 was considered the threshold of statistical significance.

## 3. Results

### 3.1. Baseline characteristics

Overall, 116 patients treated with cRP for omPCa on PSMA-PET were evaluated. The median age at diagnosis was 66 (IQR 60–72) yr, and the median PSA was 14 (IQR 7–46) ng/ml (Table 1). Of the men, 88% ($n$ = 102) had Gleason grade group (GG) ≥3 disease at biopsy; 14 (12%) patients had GG 3, 48 (41%) had GG 4, and 40 (34%) had GG 5. In general, nearly all patients had good performance status, with 111 (96%) having Eastern Cooperative Oncology Group score of ≤1. In our cohort, 70 (60%) patients underwent prebiopsy prostate MRI and 67 (96%) had PI-RADS ≥4 lesions.

In total, 102 (88%) patients were staged using PSMA-PET/CT and 14 (12%) using PSMA-PET/MRI (Table 2). In 80 (69%) men, the tracer was 68Ga-PSMA, and in 36 (31%), 18F-PSMA. Overall, 65 (56%) patients had miN1 on PSMA-PET in whom the median number of positive pelvic lymph node lesions was 3 (IQR 2–5). Most patients ($n$ = 95, 82%) were staged as miM1b, followed by 18 (16%) patients staged as miM1a and three (2.6%) as miM1c. The median number of metastases detected on PSMA-PET was 2 (IQR 1–4); 38 (33%), 29 (25%), and 49 (42%) patients had one, two, and three or more positive distant metastatic spots on PSMA-PET, respectively.

Overall, 79 (68%) patients also underwent baseline conventional imaging; 33 (28%) were staged as cM0, 14 (12%) as cM1a, and 32 (28%) as cM1b. In our oligometastatic cohort, PSMA-PET performed after conventional imaging resulted in disease upstaging in 44 (56%) patients. Overall, 33 (28%) patients underwent second PSMA-PET following neoadjuvant systemic therapy, which showed a subjective response in 28 (85%) patients; in ten (30%) patients, there was downstaging to miM0 disease (Supplementary Table 1).

### 3.2. Therapy and pathologic analyses

In our study, 70 (60%) men received neoadjuvant systemic therapy prior to cRP, which was started on median 4 (IQR 1–7) months before radical prostatectomy (RP; Table 3). Neoadjuvant therapy included androgen deprivation therapy (ADT) alone in 45 (64%) men, ADT plus docetaxel in seven (10%) men, and ADT plus ARSI in 18 (26%) men. Robot-assisted or laparoscopic cRP was performed in 66 (57%) patients; in 50 (43%) patients, the open approach was used, which was mostly center specific—three centers performed 96% ($n$ = 48) of all open surgeries. A total of 72 (62%) men underwent extended PLND. The median operating time was 175 (IQR 120–220) min and the median blood loss was 250 (IQR 150–385) ml. The median number of nodes removed was 18 (IQR 10–25, range: 1–136); 51 (44%) patients were diagnosed with pN+ disease, of whom 84% had miN1 and they harbored on a median of 3 (IQR 2–6) pathologically confirmed lymph nodes (range: 1–79). Overall, 72 (63%) men had GG ≥4 disease at final pathology, and in 19 (17%) men, GG could not be assessed because of the effect of systemic therapy. A pathologic stage of ≥pT3 was present in 94 (81%) patients at final pathology. The rate of positive surgical margins (PSMs) was 49% ($n$ = 57). Adjuvant or salvage radiation was performed in 43 (37%) patients, and 37 (32%) men received MDT. In total, 102 (88%) men were treated with neoadjuvant and/or postop

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

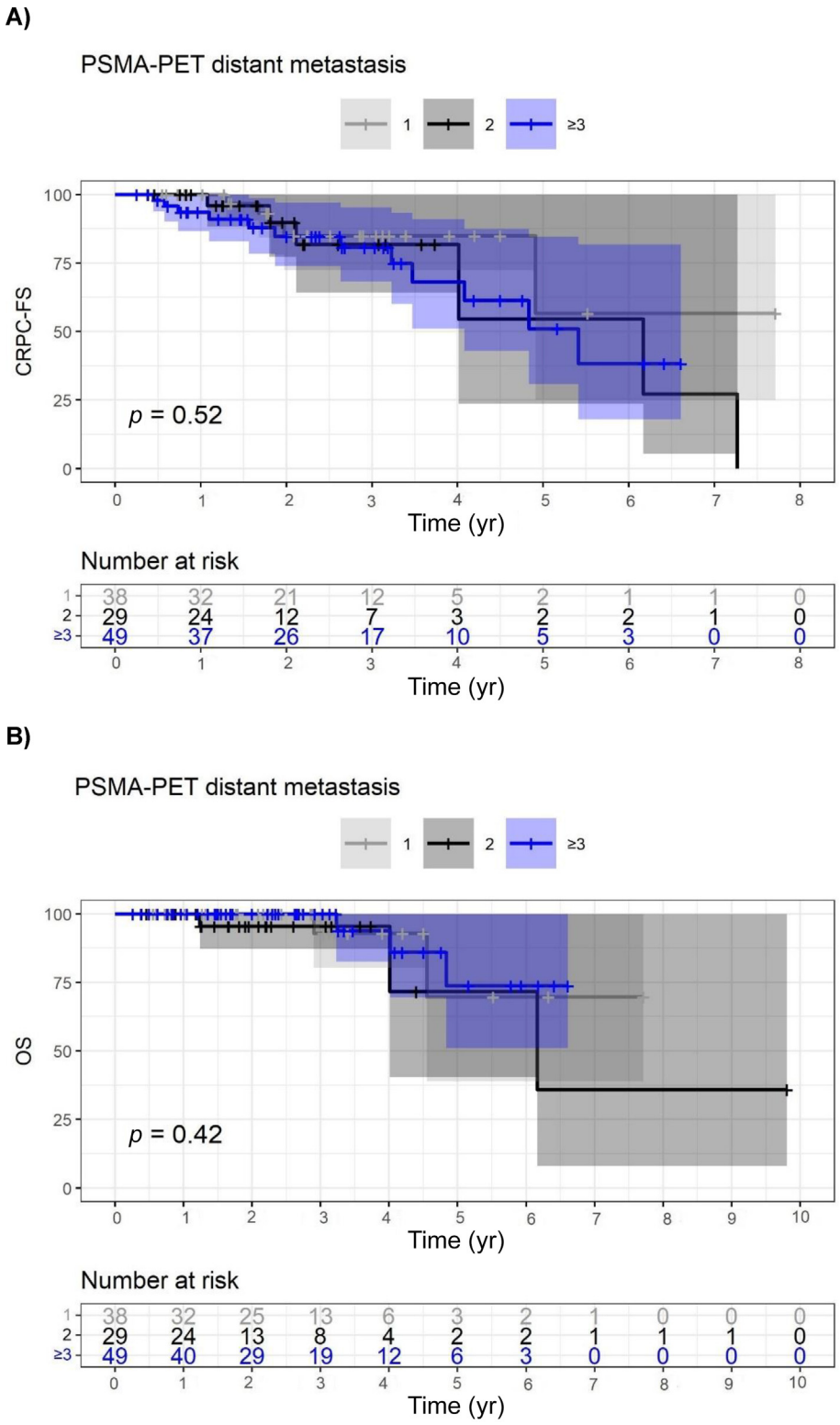


**Fig. 2 – Survival outcomes of patients treated with cRP for omPCa diagnosed using PSMA-PET according to the number of distant metastases: (A) CRPC-FS, (B) OS, and (C) rPFS. cRP = cytoreductive radical prostatectomy; CRPC-FS = castration-resistant prostate cancer–free survival; omPCa = oligometastatic prostate cancer; OS = overall survival; PET = positron emission tomography; PSMA = prostate-specific membrane antigen; rPFS = radiographic progression-free survival.**

systemic therapy. Fourteen (12%) men did not receive systemic therapy over the follow-up period; however, three (25%) of them received MDT, leaving 11 (9.5%) men who received cRP plus PLND followed by observation only.

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

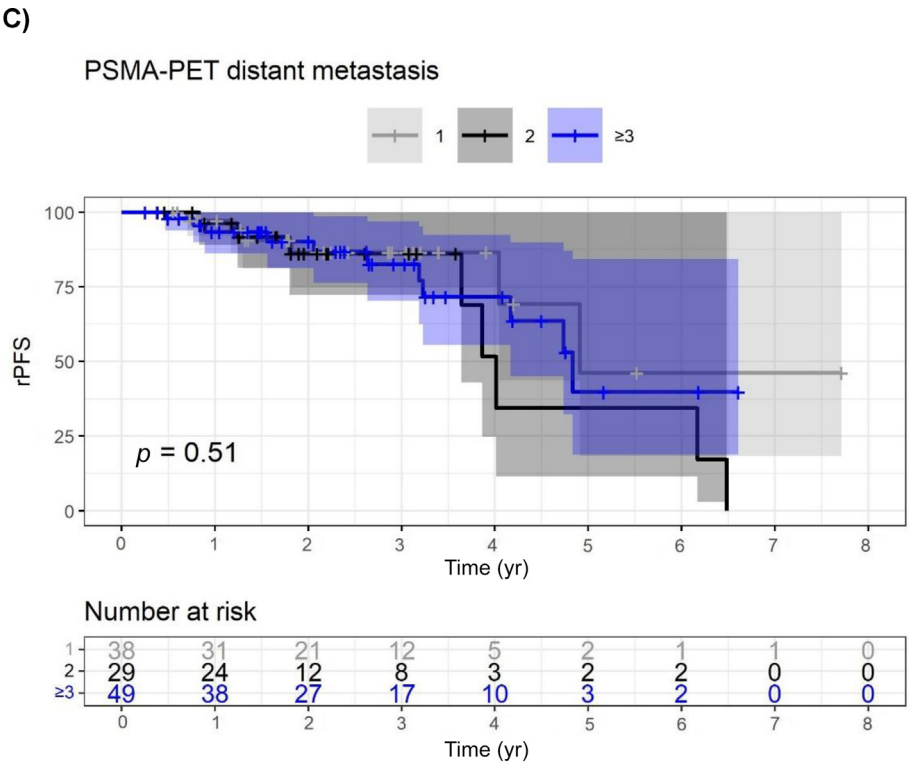


**Fig. 2** (*continued*)

### 3.3. Outcomes

Table 3 shows that 30-d complications were noted in 36 (31%) patients and six (5%) had Clavien-Dindo 3 complications requiring further reoperation, which included a lymphocele in three patients, ureteral injury treated with ureteroneocystostomy in one patient, inability to remove urinary catheter without general anesthesia due to incrustation in one man, and an anastomosis leak in one patient (Supplementary Table 2). At final observation, 82 (77%) men were continent; for the 91 patients with sufficient follow-up and available data, the 1-yr urinary continence rate was 82% ($n = 75$ continent).

The median follow-up was 27 (IQR 16–39, range: 3–118) mo. Overall, 19 (16%) patients progressed to CRPC during follow-up. Figure 1 and Supplementary Table 3 show that estimated CRPC-FS rates were 97.3% (95% CI 94.3–100%) at 1 yr, 85.8% (95% CI 78.5–93.7%) at 2 yr, and 82.2% (73.9–91.5%) at 3 yr. In patients who developed CRPC, the median time to CRPC was 22 (range 5–87) mo. Any radiographic progression was determined in 20 (17%) patients; 1-, 2-, and 3-yr rPFS rates were 95.3% (95% CI 91.3–99.4%), 87.9% (95% CI 81.4–95%), and 84.5% (95% CI 76.8–93%), respectively. Over the follow-up period, eight (7%) patients died. The 1-, 2-, and 3- OS rates were 100% (95% CI 100–100%), 98.9% (95% CI 96.8–100%), and 96.5% (95% CI 91.7–100%), respectively. In patients who died, the median time to death was 48 (range: 15–74) mo. Only two (2%) patients had local event related to PCa progression over the follow-up period. For the patients who underwent a second PSMA-PET scan after neoadjuvant systemic therapy (Supplementary Table 1), the median follow-up was 33 (IQR 25–38) mo; none died, and seven men (21%) developed CRPC.

On Kaplan-Meier estimates, there were no differences in oncologic outcomes according to the number of positive distant spots (Fig. 2) or PSMA-PET miM stage (Supplementary Table 3). Patients who had pelvic lymph node involvement at baseline PSMA-PET had worse prognosis than their miN0 counterparts (2-yr CRPC-FS: miN0: 95.4% vs miN1: 79.1%, $p = 0.01$; 2-yr rPFS: miN0: 97.4% vs miN1: 81.1%, $p = 0.08$; 3-yr OS: miN0: 100% vs 94%, $p = 0.06$; Fig. 3). Among all, 79 (68%) patients underwent conventional imaging as well; the median follow-up was 27 (IQR 14–37) mo. There were no statistically significant differences in oncologic outcomes between patients with cM0 disease at conventional imaging and those with cM1 (Fig. 4). The rates of progression to CRPC and radiographic progression were similar; however, none of the patients in the cM0 group died during the follow-up period.

In total, 105 (91%) patients were treated with additional therapies beyond cRP and PLND. Patients treated with neoadjuvant therapy had better OS (Supplementary Fig. 1). The type of neoadjuvant systemic therapy did not impact oncologic outcomes over the observation period (Supplementary Fig. 2). We did not find survival differences in patients treated or not with MDT or adjuvant/salvage RT. Supplementary Figure 3 shows that patients who reached post-cRP PSA nadir <0.1 had better CRPC-FS (estimated at 3 yr 95% vs 41%, $p < 0.001$), rPFS (estimated at 3 yr 92% vs 55%, $p = 0.002$), and OS (estimated at 3 yr 100% vs 84%, $p = 0.005$) than those with PSA nadir ≥0.1.

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

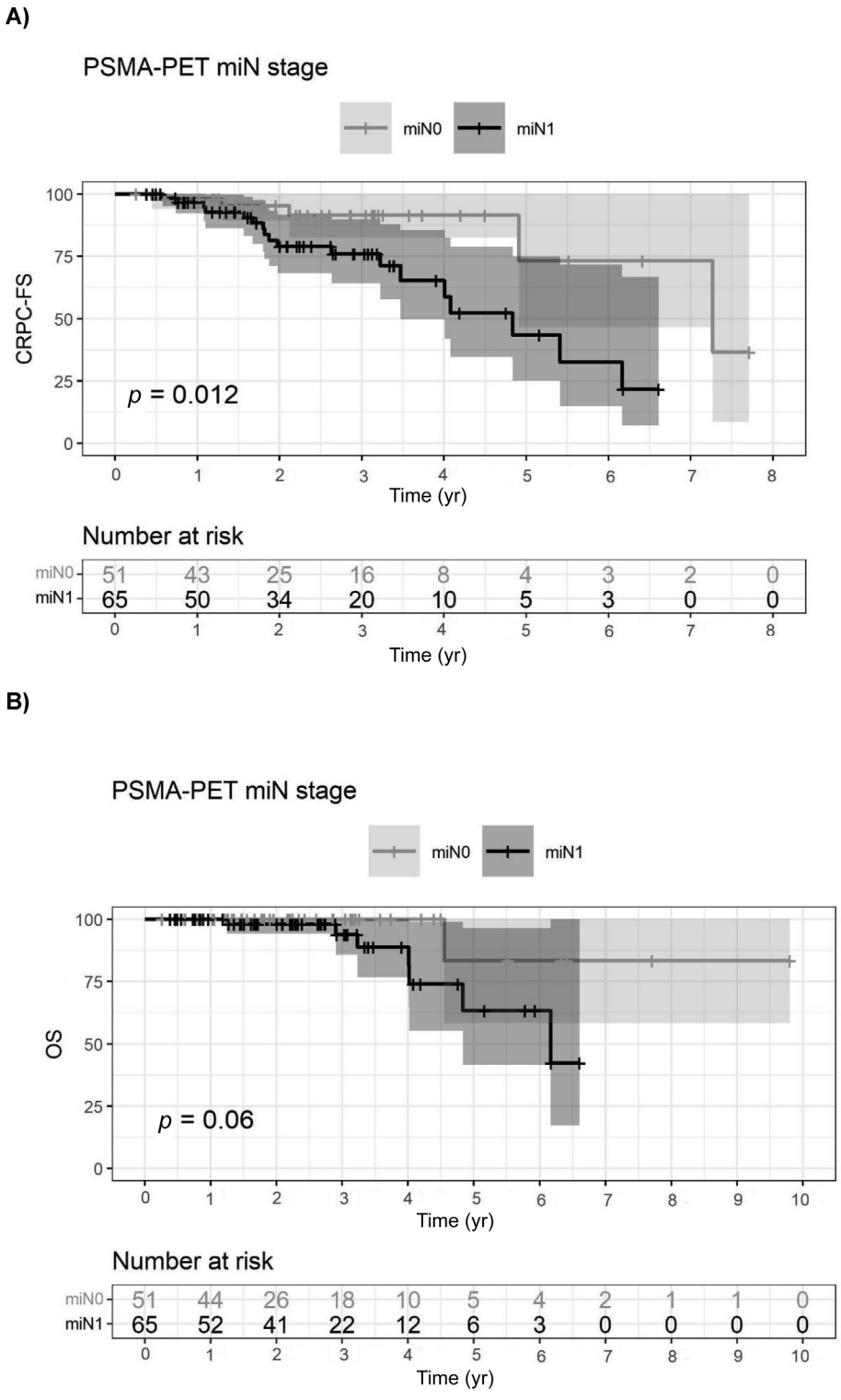


**Fig. 3 – Survival outcomes of patients treated with cRP for omPCa diagnosed using PSMA-PET according to miN stage: (A) CRPC-FS, (B) OS, and (C) rPFS. cRP = cytoreductive radical prostatectomy; CRPC-FS = castration-resistant prostate cancer–free survival; omPCa = oligometastatic prostate cancer; OS = overall survival; PET = positron emission tomography; PSMA = prostate-specific membrane antigen; rPFS = radiographic progression-free survival.**

Kaplan-Meier estimate results on the differential impact of clinicopathologic features on oncologic outcomes are shown in Supplementary Table 3; pN status, PSM, and GG at cRP had an impact on selected oncologic outcomes. Notably, only one patient who showed a pathologic response to neoadjuvant systemic therapy developed CRPC, and none died during follow-up.

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

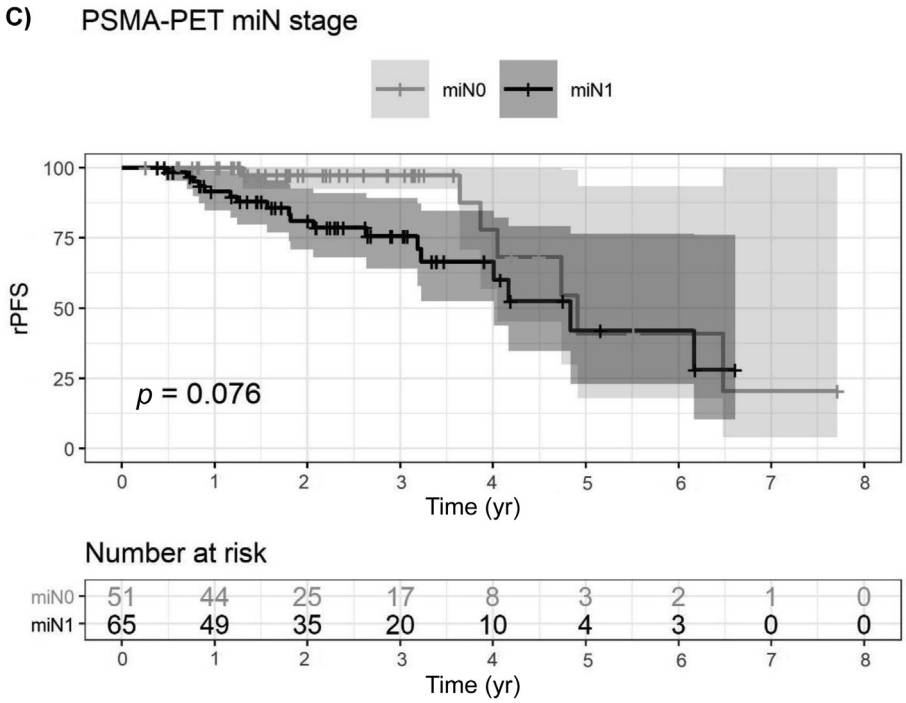


**Fig. 3** (*continued*)

### 3.4. *Univariable analysis for oncologic outcomes*

We were able to perform a univariable analysis for CRPC-FS and rPFS for several variables, which fulfilled the criteria of a sufficient number of events per subgroup/variable (Supplementary Table 4). Baseline miN status (3.64, 95% CI 1.23–10.8, $p = 0.02$) and post-cRP PSA nadir (HR 0.09, 95% CI 0.03–0.8, $p < 0.001$) were associated with CRPC-FS. The PSA response was associated with rPFS (HR 0.27, 95% CI 0.11–0.65, $p = 0.004$). Owing to a low number of deaths, we were unable to perform analyses evaluating the predictors of OS [24].

## 4. Discussion

In this study, which is the first multicenter study of its kind, we report on the outcomes of cRP in patients diagnosed with omPCa using PSMA-PET imaging. Previous studies on cRP in omPCa patients were based on those diagnosed using conventional imaging [15], and there are limited data on the oncologic outcomes of de novo omPCa diagnosed using PSMA-PET. Our findings are novel in the field of PCa, and any comparisons with other reports should be considered only theoretical and hypothesis generating.

Our study yielded several significant findings. First, we found that patients treated with cRP for omPCa diagnosed using PSMA-PET showed favorable oncologic outcomes, although there remained a notable risk of progression, even in those staged as nonmetastatic using conventional imaging. Second, our study confirmed that cRP is a safe and feasible procedure, but the pathologic findings, surgical outcomes, and functional results suggested that it is more challenging than RP in patients with nonmetastatic PCa. Third, there existed significant heterogeneity in the treatment approach among participating tertiary referral centers, with the majority of patients receiving multimodal therapy. Finally, our study identified potential predictive factors that may help tailor management and select optimal candidates for cRP among those diagnosed with omPCa using PSMA-PET.

In our cohort of patients treated with cRP for omPCa diagnosed using PSMA-PET, we report that at an estimated 2–3 yr of observation following cRP, fewer than one in five men developed CRPC and fewer than one in 20 patients died. These oncologic results appear to match or exceed those of patients treated with cRP for omPCa staged using conventional imaging. Oncologic outcomes potentially inferior to those of our cohort diagnosed on PSMA-PET were reported in the prospective PROMPT trial with a 3-yr CRPC-FS rate of 66% [25]. Sooriakumaran et al [26] analyzed 106 men with cM1a and cM1b PCa undergoing cRP; at a median follow-up of 22.8 mo, 89% of men were still alive. In our study including 116 men with a median follow-up of 27 mo, 93% of men were alive. These differences may reflect the higher sensitivity of PSMA-PET in detecting small metastatic burdens at an early stage. Notably, we did not find statistically significant differences on Kaplan-Meier survival estimates between men who were staged cM0 and cM1 on conventional imaging. These findings suggest that patients with PSMA-avid lesions that are not detectable on conventional imaging are at a substantial risk of fast disease progression to CRPC, also compared with the rates historically reported for high-risk nonmetastatic PCa [27–29]. As a result, we believe that PSMA-PET may allow for early

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

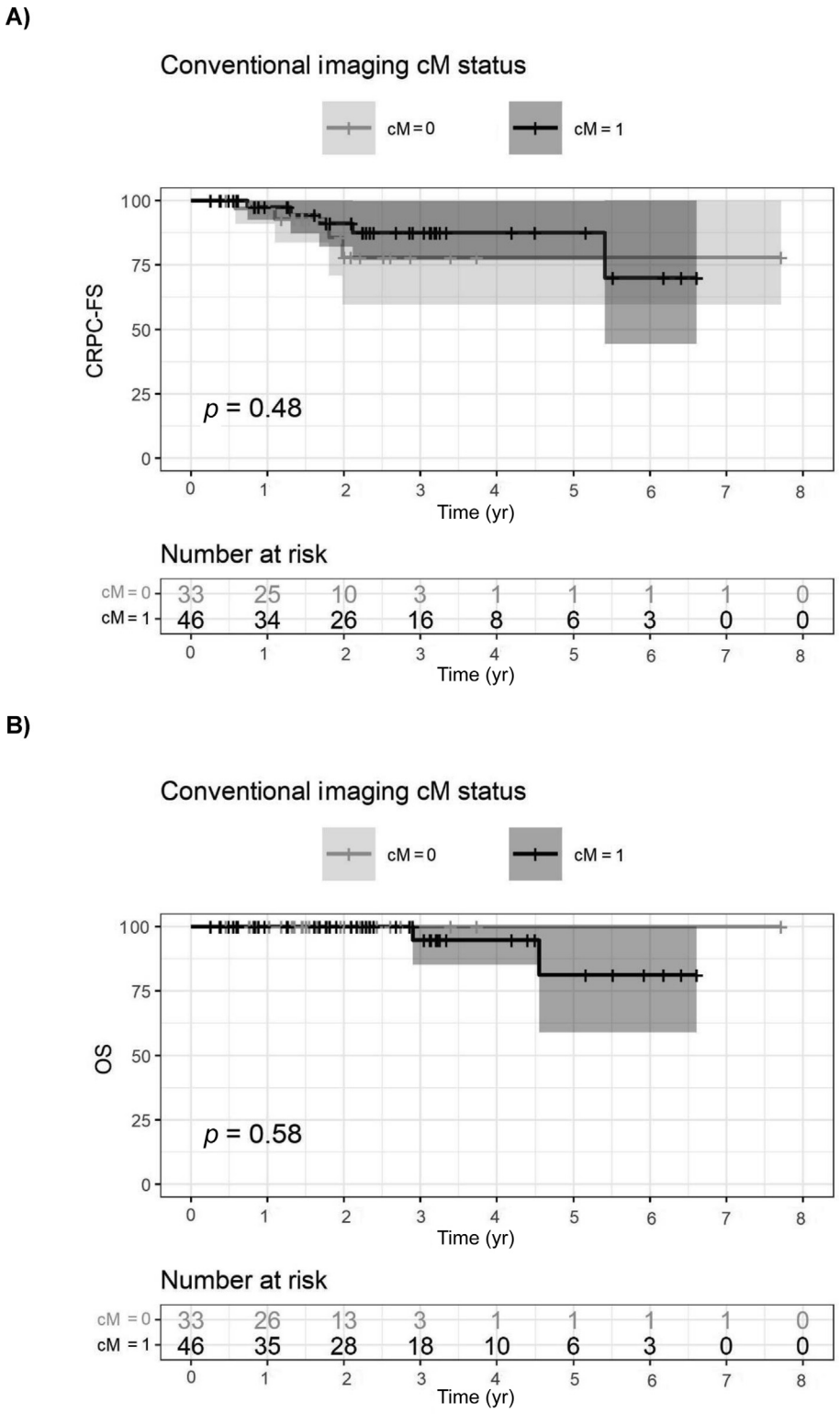


**Fig. 4 – Survival outcomes of patients treated with cRP for omPCa diagnosed using PSMA-PET according to metastasis status at conventional imaging: (A) CRPC-FS, (B) OS, and (C) rPFS. cRP = cytoreductive radical prostatectomy; CRPC-FS = castration-resistant prostate cancer–free survival; omPCa = oligometastatic prostate cancer; OS = overall survival; PET = positron emission tomography; PSMA = prostate-specific membrane antigen; rPFS = radiographic progression-free survival.**

identification and intervention, potentially altering the natural history of the disease and improving oncologic control.

In our study, the vast majority of men had locally advanced PCa with high rates of non–organ-confined dis-

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

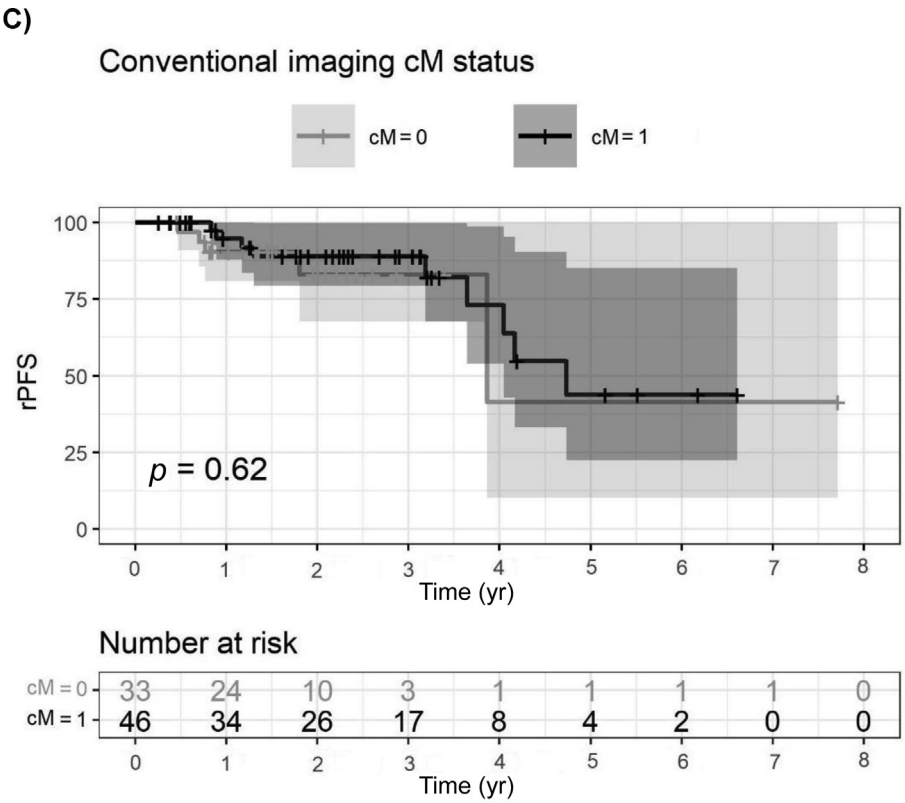


**Fig. 4** (*continued*)

ease, lymph node involvement, and dedifferentiated tumors. The approximate rates of PSM of nearly 50% and operating room time of 3 h are in line with previously reported rates in the context of cRP for omPCa staged using conventional imaging [13,14,30]. Of note, an accurate pathologic assessment might be limited in patients treated with neoadjuvant systemic therapy [31]. In our cohort, fewer than two out of five patients had any complications and only six (5%) men experienced grade 3 complications, which is again comparable with the findings of the prospective studies analyzing cRP in men diagnosed using CT/bone scan, such as the LOMP (5%) [30] or FUSCC-OMPCa trial (8%) [6], and appears to be equal to or slightly higher than in nonmetastatic setting [32]. Nevertheless, at 1-yr observation, approximately 20% suffered from incontinence (more than one pad per day), which has to be taken into account prior to cRP; these rates have also been observed in patients with nonmetastatic locally advanced disease [33].

We found large variability in treatment approaches between included centers and patients. Our study mirrors the potential lack of evidence and clinical practice guidance in omPCa patients diagnosed using PSMA-PET. While radiation therapy plus combination systemic therapy can be considered the current standard of care in omPCa patients diagnosed using conventional imaging and cRP should be regarded as an experimental approach, the true optimal management of patients with a small metastatic burden on PSMA-PET remains unknown [34]. The proper multimodal approach is especially thought provoking in patients diagnosed with cM0 disease on conventional imaging whose first-choice therapy can be RP; there is an emerging question of starting combination systemic therapies [11,35,36] and MDT [37], which seems to be more effective when guided by PSMA-PET results [38]. As a result, our study analyzing data from tertiary referral centers shows the real-life broad range of treatment efforts and escalations to cure patients diagnosed with omPCa on PSMA-PET. On the contrary, 9.5% of patients in our study received cRP plus LND only followed by low postoperative values, which further implies that patients with a very small metastatic burden and/or potential false positive lesions can be managed initially with local therapy and expectant management. In a prospective phase 2 trial, the FUSCC-OMPCa study, the authors found that patients with omPCa on conventional imaging treated with ADT plus local therapy (85% with cRP) had better 3-yr OS than patients treated with ADT alone (88% vs 70%) [6]. Therefore, there is some evidence to support cRP in the omPCa setting instead of systemic therapy alone [15]; we believe that this effect may be even stronger in patients diagnosed using molecular imaging, although without comparative studies we cannot draw solid claims yet.

Finally, although our study was underpowered to definitively determine strong predictors for favorable outcomes in men treated with cRP for omPCa diagnosed using PSMA-PET, we observed some potential prognostic factors. For instance, we found evidence for improved outcomes in men with miN0 disease or those who received neoadjuvant systemic therapy prior to cRP. Another important prognostic factor appears to be a deep PSA response following cRP,

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

which has also been associated with improved outcomes in patients with systemic therapy for metastatic hormone-sensitive PCa (mHSPC) on conventional imaging [39,40]. However, our findings should be interpreted with caution and to be validated in larger cohorts with longer follow-ups. Future research could also focus on the prognostic value of response on PSMA-PET following neoadjuvant therapy in the context of local therapy in patients with mHSPC [41].

Despite its strengths of being the first multicenter report focusing on patients treated with cRP for omPCa diagnosed using PSMA-PET, several limitations exist. First of all, this is a retrospective study without a central pathologic and imaging review; retrospective design and a lack of a central imaging review may have influenced the confidence of PSMA imaging (21% equivocal PSMA-PET results). There could be a potential selection bias, and we did not have a direct comparison arm; currently, limited available data exist on oncologic outcomes of patients treated for primary omPCa on PSMA-PET, and considering existing heterogeneity, we found it unlikely that strong propensity score matching could be performed without a significant bias at the present stage. Furthermore, there exists significant heterogeneity in the multimodal approach in the analyzed patients; however, this represents real-life management with a lack of standardized therapy in these patients. In addition, cRP was performed by multiple surgeons. In 70% of patients, imaging progression was determined using PSMA-PET imaging only, which could increase sensitivity in CRPC and radiographic progression diagnosis. We used CRPC-FS as one of the oncologic outcomes; however, we acknowledge that it is not a validated intermediate clinical endpoint in men with mHSPC. Finally, the follow-up and sample size were modest to fully explore the potential prognosis of analyzed patients with specific predictive and prognostic factors; however, the study provides relevant information to clinicians with regard to the safety, feasibility, and short-term oncologic outcomes.

## 5. Conclusions

Our study shows for the first time that over a medium-term follow-up period, patients treated with cRP for omPCa diagnosed using PSMA-PET have overall favorable oncologic outcomes. When performed in experienced, tertiary centers, cRP is safe and feasible with acceptable rates of complications and functional results. Owing to expanding treatment options targeting metastatic disease and lack of strong evidence on optimal management, in patients with omPCa staged using PSMA-PET, we found an extensive heterogeneity in multimodal approaches.

***Author contributions*:** Shahrokh F. Shariat had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

*Study concept and design*: Rajwa, Briganti, Shariat, Gandaglia.
*Acquisition of data*: Rajwa, Robesti, Chaloupka, Zattoni, Giesen, Huebner, Miszczyk, Moll, Stando, Cisero, Semko, Checcucci, Devos, Apfelbeck, Gatti, Marra, Goldner, Rasul, Ceci, Dal Moro, Porpiglia, Gontero, Stief, Heidenreich, Joniau, Briganti, Shariat, Gandaglia.
*Analysis and interpretation of data*: Rajwa, Robesti, Giesen, Miszczyk, Checcucci, Marra, Ceci, Joniau, Briganti, Shariat, Gandaglia.
*Drafting of the manuscript*: Rajwa, Shariat, Gandaglia.
*Critical revision of the manuscript for important intellectual content*: van den Bergh, Bjartell.
*Statistical analysis*: Krzywon, Rajwa.
*Obtaining funding*: None.
*Administrative, technical, or material support*: None.
*Supervision*: Briganti, Shariat.
*Other*: None.

***Financial disclosures:*** Shahrokh F. Shariat certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

***Funding/Support and role of the sponsor*:** /this study was supported by EUSP Scholarship of the European Association of Urology (Pawel Rajwa).

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euo.2023.09.006.

## References

[1] National comprehensive Cancer Network. Prostate cancer (version 1.2023). 2023. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf.
[2] Hofman MS, Lawrentschuk N, Francis RJ, et al. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. Lancet 2020;395:1208–16.
[3] Grubmuller B, Baltzer P, Hartenbach S, et al. PSMA ligand PET/MRI for primary prostate cancer: staging performance and clinical impact. Clin Cancer Res 2018;24:6300–7.
[4] Christ SM, Pohl K, Muehlematter UJ, et al. Imaging-based prevalence of oligometastatic disease: a single-center cross-sectional study. Int J Radiat Oncol Biol Phys 2022;114:596–602.
[5] Ayati N, Herrmann K, Fanti S, Murphy DG, Hofman MS. More accurate imaging is not stage migration: time to move from "hubble" to "webb" in hormone-sensitive prostate cancer. Eur Urol 2023;83:6–9.
[6] Dai B, Zhang S, Wan F-N, et al. Combination of androgen deprivation therapy with radical local therapy versus androgen deprivation therapy alone for newly diagnosed oligometastatic prostate cancer: a phase II randomized controlled trial. Eur Urol Oncol 2022;5:519–25.
[7] Parker CC, James ND, Brawley CD, et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. Lancet 2018;392:2353–66.
[8] Bernard B, Gershman B, Karnes RJ, Sweeney CJ, Vapiwala N. Approach to oligometastatic prostate cancer. Am Soc Clin Oncol Educ Book 2016;36:119–29.
[9] Rogowski P, Roach 3rd M, Schmidt-Hegemann NS, et al. Radiotherapy of oligometastatic prostate cancer: a systematic review. Radiat Oncol 2021;16:50.

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006

[10] O'Shaughnessy MJ, McBride SM, Vargas HA, et al. A pilot study of a multimodal treatment paradigm to accelerate drug evaluations in early-stage metastatic prostate cancer. Urology 2017;102:164–72.
[11] Yanagisawa T, Rajwa P, Thibault C, et al. Androgen receptor signaling inhibitors in addition to docetaxel with androgen deprivation therapy for metastatic hormone-sensitive prostate cancer: a systematic review and meta-analysis. Eur Urol 2022;82:584–98.
[12] Heidenreich A, Pfister D. Radical cytoreductive prostatectomy in men with prostate cancer and oligometastatic disease. Curr Opin Urol 2020;30:90–7.
[13] Heidenreich A, Fossati N, Pfister D, et al. Cytoreductive radical prostatectomy in men with prostate cancer and skeletal metastases. Eur Urol Oncol 2018;1:46–53.
[14] Gandaglia G, Fossati N, Stabile A, et al. Radical prostatectomy in men with oligometastatic prostate cancer: results of a single-institution series with long-term follow-up. Eur Urol 2017;72:289–92.
[15] Rajwa P, Zattoni F, Maggi M, et al. Cytoreductive radical prostatectomy for metastatic hormone-sensitive prostate cancer—evidence from recent prospective reports. Eur Urol Focus 2023;9:637–41.
[16] Fonseca NM, Van der Eecken K, Herberts C, et al. Genomic features of lung-recurrent hormone-sensitive prostate cancer. JCO Precis Oncol 2022;6:e2100543.
[17] Fendler WP, Eiber M, Beheshti M, et al. PSMA PET/CT: joint EANM procedure guideline/SNMMI procedure standard for prostate cancer imaging 2.0. Eur J Nucl Med Mol Imaging 2023;50:1466–86.
[18] Barentsz JO, Weinreb JC, Verma S, et al. Synopsis of the PI-RADS v2 guidelines for multiparametric prostate magnetic resonance imaging and recommendations for use. Eur Urol 2016;69:41–9.
[19] Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate cancer—2020 update. Part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol 2021;79:243–62.
[20] Rabbani F, Yunis LH, Pinochet R, et al. Comprehensive standardized report of complications of retropubic and laparoscopic radical prostatectomy. Eur Urol 2010;57:371–86.
[21] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.
[22] Porpiglia F, Morra I, Lucci Chiarissi M, et al. Randomised controlled trial comparing laparoscopic and robot-assisted radical prostatectomy. Eur Urol 2013;63:606–14.
[23] Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. Am J Epidemiol 2007;165:710–8.
[24] Peduzzi P, Concato J, Feinstein AR, Holford TR. Importance of events per independent variable in proportional hazards regression analysis. II. Accuracy and precision of regression estimates. J Clin Epidemiol 1995;48:1503–10.
[25] Mandel PC, Huland H, Tiebel A, et al. Enumeration and changes in circulating tumor cells and their prognostic value in patients undergoing cytoreductive radical prostatectomy for oligometastatic prostate cancer—translational research results from the prospective ProMPT trial. Eur Urol Focus 2021;7:55–62.
[26] Sooriakumaran P, Karnes J, Stief C, et al. A multi-institutional analysis of perioperative outcomes in 106 men who underwent radical prostatectomy for distant metastatic prostate cancer at presentation. Eur Urol 2016;69:788–94.
[27] Wilt TJ, Jones KM, Barry MJ, et al. Follow-up of prostatectomy versus observation for early prostate cancer. N Engl J Med. 2017;377:132–42.
[28] Lei JH, Liu LR, Wei Q, et al. Systematic review and meta-analysis of the survival outcomes of first-line treatment options in high-risk prostate cancer. Sci Rep 2015;5:7713.
[29] Zelefsky MJ, Eastham JA, Cronin AM, et al. Metastasis after radical prostatectomy or external beam radiotherapy for patients with clinically localized prostate cancer: a comparison of clinical cohorts adjusted for case mix. J Clin Oncol 2010;28:1508–13.
[30] Buelens S, Poelaert F, Claeys T, et al. Multicentre, prospective study on local treatment of metastatic prostate cancer (LoMP study). BJU Int 2022;129:699–707.
[31] Evans AJ. Treatment effects in prostate cancer. Mod Pathol 2018;31:110–21.
[32] Pompe RS, Beyer B, Haese A, et al. Postoperative complications of contemporary open and robot-assisted laparoscopic radical prostatectomy using standardised reporting systems. BJU Int 2018;122:801–7.
[33] Gandaglia G, De Lorenzis E, Novara G, et al. Robot-assisted radical prostatectomy and extended pelvic lymph node dissection in patients with locally-advanced prostate cancer. Eur Urol 2017;71:249–56.
[34] Mottet N, Conford P, van den Bergh RCN, et al. EAU - EANM - ESTRO - ESUR - ISUP - SIOG guidelines on prostate cancer. EAU Guidelines Office; 2022. https://uroweb.org/guidelines/prostate-cancer.
[35] Dhiantravan N, Violet J, Eapen R, et al. Clinical trial protocol for LuTectomy: a single-arm study of the dosimetry, safety, and potential benefit of $^{177}$Lu-PSMA-617 prior to prostatectomy. Eur Urol Focus 2021;7:234–7.
[36] Rajwa P, Pradere B, Gandaglia G, et al. Intensification of systemic therapy in addition to definitive local treatment in nonmetastatic unfavourable prostate cancer: a systematic review and meta-analysis. Eur Urol 2022;82:82–96.
[37] Rajwa P, Yanagisawa T, Gruber M, et al. Surgical metastasectomy for visceral and bone prostate cancer metastases: a mini-review. Eur Urol Focus 2023;9:232–5.
[38] Phillips R, Shi WY, Deek M, et al. Outcomes of observation vs stereotactic ablative radiation for oligometastatic prostate cancer: the ORIOLE phase 2 randomized clinical trial. JAMA Oncol 2020;6:650–9.
[39] Hussain M, Tangen CM, Higano C, et al. Absolute prostate-specific antigen value after androgen deprivation is a strong independent predictor of survival in new metastatic prostate cancer: data from Southwest Oncology Group Trial 9346 (INT-0162). J Clin Oncol 2006;24:3984–90.
[40] Choueiri TK, Xie W, D'Amico AV, et al. Time to prostate-specific antigen nadir independently predicts overall survival in patients who have metastatic hormone-sensitive prostate cancer treated with androgen-deprivation therapy. Cancer 2009;115:981–7.
[41] Esen B, Herrmann K, Bavbek S, Kordan Y, Tilki D, Esen T. Prostate-specific membrane antigen positron emission tomography as a biomarker to assess treatment response in patients with advanced prostate cancer. Eur Urol Focus 2023;9:596–605.

Please cite this article as: P. Rajwa, D. Robesti, M. Chaloupka et al., Outcomes of Cytoreductive Radical Prostatectomy for Oligometastatic Prostate Cancer on Prostate-specific Membrane Antigen Positron Emission Tomography: Results of a Multicenter European Study, Eur Urol Oncol (2023), https://doi.org/10.1016/j.euo.2023.09.006