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Oncological long-term outcome of 4772 patients with prostate cancer undergoing radical prostatectomy: Does the anaesthetic technique matter?

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Abstract

Introduction: Recent data suggest that using additional neuroaxial anaesthesia during oncological surgery is associated with favourable recurrence-free survival, when compared with general anaesthesia alone. We assessed the impact of adjunctive perioperative spinal anaesthesia and dose of opioids on the oncological long-term outcome of patients following radical prostatectomy.
Methods: We selected patients from our institutional review board-approved database who consecutively underwent radical prostatectomy between 2002 and 2007. Patients were stratified by type of anaesthesia, administered as general anaesthesia alone, or spinal anaesthesia in addition to general anaesthesia. Biochemical recurrence-free survival, metastasis-free survival and overall survival were analysed by a multivariate Cox regression model and by Kaplan–Meier analysis in propensity-score based matched cohorts, adjusted for standard clinico-pathological variables and year of surgery.
Results: Overall, 4772 patients were analysed. Regarding the type of anaesthesia no significant difference for biochemical recurrence-free survival, metastasis-free survival and overall survival was analysed by a multivariate Cox regression model ($p = 0.5$, 0.8 and 0.7). The Kaplan–Meier analyses after propensity-score matched based comparisons revealed no significant difference depending on type of anaesthesia for biochemical recurrence-free survival, metastasis-free survival and overall survival ($p = 0.6$, 0.1 and 0.4). The same accounted for a propensity-score matched model adjusted for the year of surgery on biochemical recurrence-free survival ($p = 0.7$).
Conclusions: The oncological outcome after radical prostatectomy was not affected by the adjunctive use of spinal anaesthesia.

Keywords: Prostate cancer; Oncological outcome; Regional anaesthesia; Tumour control; Radical prostatectomy

Introduction

The biological rationale for a potential impact of regional anaesthesia on cancer control is that surgery inevitably induces a neuroendocrine, metabolic and cytokine response, resulting in transient immunosuppression in the vulnerable perioperative period.[1] Additional immunosuppressive effects are supposed for intraoperatively administered opioids.[1] The perioperative period is of particular relevance regarding scattered tumour cells, which have disseminated during surgery and might be controlled by the immune system.[1–3] Regional, and in particular neuraxial anaesthesia leads to a reduced neuroendocrine stress response to the surgical trauma and a lower intraoperative use of opioids.[1,4]

Prostate cancer (PCa) is the most common malignancy in men accounting for more than 600,000 diagnosed cases in the United States and Europe, annually.[5,6] In the majority of cases with localized disease, radical prostatectomy

Abbreviations: PCa, prostate cancer; RP, radical prostatectomy; SPA, spinal anaesthesia; SGA, combination of spinal anaesthesia and general anaesthesia; GA, general anaesthesia; BCR, biochemical recurrence; BFS, biochemical recurrence-free survival; MFS, metastasis-free survival; OS, overall survival.

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(RP) is the treatment of choice.[7,8] Therefore, data, suggesting a potential effect of adjunctive neuraxial anaesthesia on cancer control after RP are of a particular high clinical importance.

Previous studies, assessing the oncological outcome after the use of adjunctive regional anaesthesia and reduction of systemically given opioids in the surgical treatment of PCa, colon cancer, and breast cancer revealed contradictory results.[9–19]

Based on the high relevance of the subject for oncologic surgery we tested the hypothesis that combined general anaesthesia and spinal anaesthesia improve cancer control compared to general anaesthesia alone in 4772 consecutive patients who underwent a highly standardized surgery in a single high-volume surgical centre.

Methods

Patient selection

Overall, 4917 consecutive patients who underwent RP in our institution between 2002 and 2007 were analysed. All data were collected prospectively into an institutional review board-approved database. Overall, 145 patients were excluded from analyses due to other surgical techniques (laparoscopic RP, perineal RP; $n = 106$), missing data ($n = 37$), or vanishing cancer ($n = 2$). The remaining 4772 patients were subject of this study. RP was performed using an open retropubic approach as previously described.[20–22] The patients where stratified by type of anaesthesia: 3047 patients underwent spinal anaesthesia (SPA) in addition to general anaesthesia (SGA) and 1725 patients general anaesthesia (GA) alone. Total intravenous anaesthesia (TIVA) was administered more frequently within the SGA group (98 vs. 10%). Additionally, higher blood transfusion rates were documented within the GA patients compared to SGA (20.3 vs. 3.4%, $p < 0.001$) Biochemical recurrence (BCR) was defined as a PSA value $\geq$0.2 ng/ml after RP. Metastases were defined as positive MRI, CT or bone scan results, indicated on the discretion of the physician in charge. Radiation therapy and androgen deprivation therapy within 6 month after surgery were considered as adjuvant treatment. Overall, 3 (0.2%), 19 (1.1%), and 7 (0.4%) of the GA, and 15 (0.5%), 71 (2.3%), and 22 (0.7%) of the SGA patients received an adjuvant radiation therapy or adjuvant androgen deprivation or a combination of both, respectively ($p < 0.001$). The distribution of adjuvant treatments between the two groups were not anymore significant after propensity score matching (all $p > 0.05$). The study was approved by the local ethics committee of the Medical Board Hamburg (WF-038/10).

Perioperative anaesthesiological management

Before 2003 standard anaesthesiological management for RP was GA. Since 2003 standard for anaesthesiological management is SGA in order to decrease perioperative morbidity and to optimize immediate postoperative pain management. If contraindications for SPA are not present, a single shot SPA is performed prior to induction of GA. Therefore a height adapted injection of 3–4 ml Bupivacaine 0.5% isobar and sufentanil 5 μg in the subarachnoid space in location of lumbar spine 3/4 or 4/5 is performed. GA is then induced with sufentanil (0.3–0.5 μg/kg) in combination with propofol (2 mg/kg) and, if necessary, rocoroniumbromide (0.6 mg/kg) for neuromuscular blockade. GA is performed as total intravenous anaesthesia with propofol (5–8 mg/kg/h), or as balanced anaesthesia with inhaled isoflurane or sevoflurane. If indicated, intraoperatively repeated bolus injections of sufentanil or rocoroniumbromide are administered.

Table 1
Baseline characteristics of the patient cohort.

Parameter	Overall	SGA (%)	GA (%)	*p* Value
Patients	4772	3047 (63.9)	1725 (36.1)	
Preoperative PSA [ng ml^{-1}]				
<4	822	479 (15.8)	343 (19.9)	<0.001
4–10	2960	1952 (64.4)	1008 (58.5)	
10–20	797	482 (15.9)	315 (18.3)	
>20	172	116 (3.8)	56 (3.3)	
pT-stage				
pT2	3531	2224 (73.2)	1307 (75.9)	0.1
pT3a	868	580 (19.1)	288 (16.7)	
pT3b	361	234 (7.7)	127 (7.4)	
pN-status				
NX	3102	1764 (58.1)	1338 (78.0)	<0.001
pN0	1505	1162 (38.3)	343 (20.0)	
pN1	145	111 (3.7)	34 (2.0)	
Gleason score				
≤3 + 3	1961	1114 (36.9)	847 (49.5)	<0.001
3 + 4	2137	1447 (47.9)	690 (40.3)	
4 + 3	517	371 (12.3)	146 (8.5)	
≥4 + 4	119	91 (3.0)	28 (1.6)	
Surgical margin				
R0	3988	2576 (84.5)	1412 (81.9)	0.02
R1	783	471 (15.5)	312 (18.1)	
Sufentanil (μg)				
Mean ± s.d.	45.5 ± 20.1	34.2 ± 11.1	65.3 ± 16.9	<0.001
Median (IQR)	40 (30–60)	30 (25–40)	65 (55–75)	
Range	0–180	0–100	20–180	

Statistical analysis

Baseline characteristics between GA and SGA patients were compared using the chi^2 likelihood test for nominal variables and the non-parametric Wilcoxon test for continuous variables. We investigated the effect of the use of an SGA compared to GA on biochemical recurrence-free survival (BFS), metastasis-free survival (MFS), and overall survival (OS) after RP utilizing multivariable Cox proportional hazard analysis and propensity-score matching analysis.[23] Propensity-score matched analysis was performed in a regression model using 1) preoperative PSA, pT-stage, RP specimen Gleason score, pN-status and margin-status and 2) as model 1 and additionally year of surgery as covariates. Based on estimated propensity-scores, one patient from the