Platinum Priority – Review – Prostate Cancer

Editorial by XXX on pp. x–y of this issue

A Systematic Review of the Impact of Surgeon and Hospital Caseload Volume on Oncological and Nononcological Outcomes After Radical Prostatectomy for Nonmetastatic Prostate Cancer

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1. Introduction

The outcomes of (oncological) surgery are closely related to the quality of the procedure and postoperative care, which is directly influenced by the proficiency of both the surgeon and the team taking care of patients. The volume of cases performed by a surgeon or an institution may be an important surrogate for these factors. There is evidence for radical cystectomy that units performing a large number of cases on a regular basis have better outcomes in terms of lower perioperative complications including mortality. It was the first procedure considered for centralisation in urological practice, and has resulted in a downward trend in complications and postoperative mortality rates [1–3].

Radical prostatectomy (RP) for prostate cancer (PCa) is associated with lower rates of immediate complications or mortality, especially when compared with radical cystectomy. However, expertise is needed, since both the negative impact of positive surgical margins (PSMs) on biochemical recurrence (BCR) [4,5] and the positive impact of neurovascular bundle preservation [6] on postoperative potency and continence are well recognised. Currently, the impact of caseload volume of RP on oncological and nononcological outcomes remains controversial. The aim of this study was to perform a systematic review to investigate the relationship between caseload volume of RP performed by hospital or individual surgeons for localised PCa, and oncological and nononcological outcomes in order to define minimum thresholds to optimise outcomes.

2. Evidence acquisition

The review was undertaken by the European Association of Urology (EAU) Prostate Cancer Guideline Panel. A protocol on the conduct of this systematic review has been published a priori online on PROSPERO (http://www.crd.york.ac.uk/PROSPERO; CRD42020186466).

Briefly, the systematic review was undertaken in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [7] and Cochrane [8] guidelines. Databases including MEDLINE, Embase, and Cochrane Database of Systematic Reviews were systematically searched for articles published in English between...
January 1, 1990 and May 8, 2020 using the search strategy shown in the Supplementary material. Men with histologically proven nonmetastatic PCA who were treatment naïve prior to recruitment were included. The index intervention was RP (any approach) performed in a higher-volume hospital/unit or by a higher-volume surgeon (defined as the number of procedures per unit time), and the comparator intervention was RP performed in a lower-volume hospital/unit or by a lower-volume surgeon. The thresholds of higher versus lower volume (eg, above/below 50 cases per year) were kept as defined by the original authors. The primary oncological outcomes were undetectable prostate-specific antigen (PSA) postoperatively, PSM, biochemical-free survival, freedom from additional therapy, distant metastasis–free survival (DMFS), PCA-specific survival (PCSS), and overall survival (OS). The secondary outcomes were nononcological outcomes, including urinary and erectile function recovery over time and perioperative complications within 90 d (including need for blood transfusion, conversion from minimally invasive to open procedure, and death). Only comparative studies (prospective and retrospective) comparing different hospital/unit/surgeon case-load volumes of RP were included; studies reporting exclusively on learning curve and previous experience were excluded. Subgroup and sensitivity analyses were planned on EAU risk groups, clinical stage, PSA levels, patient comorbidities (including body mass index), and RP approach (ie, open, laparoscopic, or robotic assisted). Risk of bias (RoB) and confounding assessment was performed using the standard Cochrane RoB tool designed for randomised controlled trials modified to include additional confounders relevant to nonrandomised comparative studies. Abstract and full-text screening, data extraction, and RoB and confounding assessments were performed independently in duplicate (D.O., T.V.D.B., M.K., and L.M.), and disagreement was resolved by discussion or reference to an independent third party (T.V.D.B. and L.M.). Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment was performed to evaluate the quality of evidence. A qualitative synthesis was primarily planned due to the expected clinical and methodological heterogeneity of included studies; however, if the data allowed, a formal meta-analysis would be performed.

3. Evidence synthesis

3.1. Quantity of evidence identified

The study selection process is outlined in the PRISMA flow diagram (Fig. 1). Sixty retrospective comparative studies were included [9–68]. The commonest reasons for exclusion were the following: (1) Inappropriate definition of surgical/hospital volume, and (2) irrelevant outcomes reported.

3.2. RoB and confounding assessment

Figures 2A–D summarise the results of the RoB and confounding assessments. Owing to the retrospective nature of all studies, most studies were judged to have high RoB for most domains. The risk of confounding was high for most domains for studies correlating hospital volume with oncological and nononcological outcomes, and for studies correlating surgical volume with nononcological outcomes.

3.3. Characteristics of included studies and summary of results

Supplementary Tables 5–8 present the baseline characteristics of included studies and Supplementary Tables 1–4 present the results for all studies. Results were stratified by surgeon or hospital volume, and by oncological or nononcological outcomes. Studies reporting on both surgeon- and hospital-related outcomes or on both oncological and nononcological outcomes are marked by three asterisks (**). A meta-analysis could not be performed due to the retrospective, nonrandomised nature of included studies and their observed clinical heterogeneity across studies, in particular regarding the definition of high versus low volume. Owing to this heterogeneity, the predefined comparison of predefined cut-offs (10, 20, and 50 annual caseload) was impossible, and volumes were reported as defined by the authors. For the studies that performed multivariate logistic regression analyses and reported odds ratios (ORs), solely to provide a visual summary, the results were displayed using forest plots (without including a pooled estimate). Patients and tumour characteristics were highly heterogeneous across all studies, and often reported poorly or not reported at all. This is also reflected by the moderate to high risk of confounders. An interpretation of the patient characteristics was therefore avoided for the studies that did not attempt to correct for any essential covariates for their respective outcomes. Only the studies that attempted such corrections in their model were included in the forest plots for interpretation. The covariables for each individual study are summarised in Supplementary Tables 1–4 under the column heading “Corrected for (if MVA)”.

3.3.1. Characteristics of included studies on hospital volume

3.3.1.1. Oncological outcomes

3.3.1.1.1. Positive surgical margins. Six studies evaluated the impact of hospital volume on the presence of a PSM in the final pathology report after RP [10,11,24,33,50,55]. Two studies performed a multivariable logistic regression analysis, comparing hospitals with increasing volume (Fig. 3), showing a reduction in the number of PSMs with increasing hospital volume when comparing with low-volume hospitals [10,11]. Compared with hospitals with the lowest volume, hospitals with the highest volume have a reported OR for PSMs between 0.83 (95% confidence interval [CI] 0.70–0.99) and 0.61 (95% CI 0.59–0.64). Comparable results are reported by Evans et al [50], who reported a relative risk for PSMs of 1.44 (95% CI 1.07–1.93) when comparing low- with high-volume hospitals. Two studies do not show a significant association between hospital volume and PSMs, but differ from the other studies by not comparing the hospitals with the lowest and highest
volumes [33,55]. Taken together, these data suggest that centres with high caseload volume of RP have lower rates of PSMs when compared with centres with low volume. The three studies [10,11,50] showing this association defined a low-volume hospital as a hospital with an annual caseload volume of three to 45, <89, and fewer than ten procedures.

3.3.1.2. Other oncological outcomes. Six studies investigated the association of hospital volume with BCR [25,60], need for adjuvant radiotherapy [37], DMFS [60], PCSS [25,51,65], and OS [51,61]. Clearly, only limited data were available, which were mostly inconclusive. The two studies on BCR showed conflicting results with those of O’Kane et al [25] due to lower rates of BCR in high-volume centres (>80 cases per year) versus low-volume centres (<80 cases per year) with a hazard ratio (HR) of 0.84 (p = 0.036), whilst Baunacke et al [60] showed very similar BCR rates between different hospital volume groups, ranging between 19% and 25% at 6 yr of follow-up. One study, which investigated the use of adjuvant therapies [37], showed that patients treated at high-volume hospitals (43–1110 cases per year) have an OR of 0.47 (95% CI 0.42–0.52) to receive adjuvant radiotherapy compared with low-volume hospitals (one to six cases per year). For DMFS, Baunacke et al [60] did not report a difference in outcome. Lastly, for both PCSS and OS, conflicting results exist, with two studies showing an association [61,65] and two studies showing no association [25,51] with hospital volume.

3.3.1.2. Nononcological outcomes

3.3.1.2.1. Complications. Fourteen studies [9,12,20,26,27,29,30,34,38,44,48,55,59,68] reported on the association of annual caseload volume with overall intra- and postoperative complications. Eight out of these 14 studies showed a significant association with the reduction in complication rates, with increasing annual caseload volume [9,20,26,30,44,48,59,68] (Fig. 4). Five studies [12,27,34,38,55] did not find any statistically significant differences, whilst in one study [29] the authors did not...
Fig. 2 – (A) Risk of bias assessment for studies on hospital volume–nononcological outcomes. *** Study included in another table as well. (B) Risk of bias assessment for studies on hospital volume–oncological outcomes. *** Study included in another table as well. (C) Risk of bias assessment for studies on surgeon volume–nononcological outcomes. *** Study included in another table as well. (D) Risk of bias assessment for studies on surgeon volume–oncological outcomes. *** Study included in another table as well. BMI = body mass index; iPSA = initial prostate-specific antigen.
report a statistical analysis. Out of the five studies that did not show a significant difference, two did not perform a multivariable analysis [34,55], and although complication rates were numerically the lowest in the highest-volume group in the study of Chan et al [55], it was not statistically significant. These results, and the forest plots summarising all multivariable analyses (Fig. 4–6), indicate a clinically relevant association between hospital caseload volume and peri- and postoperative complications after RP. One study by Barashi et al [62] showed a significantly lower odds of perioperative rectal laceration for high-volume (>43 cases per year) versus low-volume (one to 43 cases per year) hospitals with an OR of 0.58 (95% CI 0.46–0.72). One study showed significantly lower odds of postoperative venous thromboembolisms in high- versus low-volume hospitals [54]. Three studies unanimously reported higher odds of open conversion during minimally invasive RP (MIRP) for low-volume hospitals (Fig. 5) [10,31,43]. Finally, eight studies reported on blood transfusion rates. Five of these performed multivariable analysis and all five showed increased odds of needing blood transfusion for lower-volume hospitals (Fig. 6) [19,46,48,55,68]. The remaining three studies reported raw numbers showing lower transfusion rates with increasing hospital volume [9,34,36].

3.3.1.2.2. Perioperative mortality. Thirteen studies [10,26,29,30,35,38,42,45–47,59,64,68] reported on peri- and postoperative mortality, of which eight studies performed multivariable logistic regression analysis (Fig. 7) [26,38,42,45–47,64,68], and one study performed univariable logistic regression analysis [35]. All but one study showed a lower rate of mortality with increasing hospital volume [64]. Interestingly, the study by Gilbert et al [47] showed that the observed effect was countered when the analysis was corrected for general urological oncology volume, suggesting that in hospitals where other urological surgery is performed routinely, the expertise in peri- and postoperative care negates the effect of lower annual volume of this specific surgery. As shown by four independent studies, mortality rates are low after RP [10,29,30,59]. Statistically significant differences in raw numbers are therefore unlikely, particularly with the moderate sample size in these studies. Mitchell et al [30], in a study with 48,086 included patients, showed significantly lower rates of in-hospital mortality in the high-volume subgroup (>111 cases per year), with mortality rates of 0.02% compared with 0.15% for the low-volume subgroup (zero to 22 cases per year). Although no statistical comparison was performed, in the studies conducted by Xia et al [10] and Nathan et al [29], 90- and 30-d mortality rates, respectively, were lowest in the high-volume subgroups: (≥219 cases per year for Xia et al [10] and 22–243 cases per year for Nathan et al [29]). Begg et al [59] showed similar 30- and 60-d mortality rates ranging from 0.5% to 0.6%, which is relatively high compared with other reported studies.

3.3.1.2.3. Urinary incontinence. Two studies reported on postoperative urinary incontinence with conflicting results. Baunacke et al [60] showed better continence rates with increasing hospital volume, ranging from 72% to 89% for the lowest (zero to 19 cases per year) to the highest (>200 cases per year) hospital volume subgroups, whilst Begg et al [59] showed similar rates of long-term incontinence of >1 yr, ranging from 18% to 19% irrespective of hospital volume.
Hospital volume – positive surgical margins

Fig. 3 – Forest plot summarising the evidence on the association of hospital volume and positive surgical margins.

Hospital volume - Complications

Fig. 4 – Forest plot summarising the evidence on the association of hospital volume and peri- and postoperative complications.
3.3.1.2.4. Potency. Only one study conducted by Baunacke et al [60] reported on postoperative potency (defined as an erection firm enough for sexual intercourse) and showed significantly higher potency rates for high-volume hospitals with 6% versus 6% versus 8% versus 11% versus 22% in hospitals with an annual volume of 0–19, 20–49, 50–99, 100–199, and ≥200, respectively.

3.3.2. Characteristics of included studies on surgeon volume

3.3.2.1. Oncological outcomes
3.3.2.1.1. Positive surgical margins. Six studies evaluate the impact of surgeon volume on the presence of PSMs at the final pathology report after RP [13,22,23,28,32,67]. Five studies performed a multivariable logistic regression analysis (Fig. 8). Porcaro et al [22,23] published two...
manuscripts, one investigating PSMs overall and one subdividing focal positive (≤1 mm) and nonfocal (>1 mm) PSMs. Their data show an association in the overall cohort with high-volume surgeons having lower rates of PSMs with an OR of 0.61 (95% CI 0.43–0.87). Interestingly, this effect was accentuated in their subgroup study with an OR of 0.57 (95% CI 0.39–0.86), whilst this association was not statistically significant for the subgroup of nonfocal PSMs with an OR of 0.71 (95% CI 0.41–1.1). Steinsvik et al [13] also showed an increase in PSMs for lower-volume surgeons with an OR of 1.83 (95% CI 1.02–3.30) for intermediate-volume (20–50 cases per year) and 3.73 (95% CI 2.25–6.17) for low-volume (<20 cases per year) surgeons compared with high-volume (>50 cases per year) surgeons. In contrast, Nayak et al [28] reported an inverse association with higher rates of PSMs for high-volume surgeons. They argue that their findings are due to the small number of surgeons practising in the investigated region.

Fig. 7 – Forest plot summarising the evidence on the association of hospital volume and peri- and postoperative mortality rates.

Fig. 8 – Forest plot summarising the evidence on the association of surgeon volume and positive surgical margins.
Lastly, Williams et al. [32] could not find an association of surgeon volume and PSMs. Overall, especially when contrasted with the observed effects of hospital volume, the evidence for association between surgical annual volume and PSMs is not very persuasive.

3.3.2.1.2 Other oncological outcomes. Eight studies investigated the association of surgeon volume with survival endpoints, including BCR [14,22,67], need for adjuvant/salvage therapies [21,39,40,53], and PCSS [58]. Two of three studies reporting on BCR did not show an association with surgical volume [14,22]. A study by Vesey et al. [67] plotted the risk of BCR against annual surgical case volume and described a trend towards improved outcomes with increasing volume, particularly for volumes in excess of 15 cases annually. All four studies that reported on additional cancer-related therapies show a significant association with surgical annual volume. Williams et al. [21] reported significantly lower odds to receive additional cancer treatment within 6 mo after RP for very high-volume (open RP [ORP]: 30–91 cases every 2 yr; MIRP: 90–128 cases every 2 yr) compared with those for low-volume (ORP: one to seven cases every 2 yr; MIRP: one to 14 cases every 2 yr) surgeons with an OR of 0.60 (95% CI 0.46–0.78). Hu et al. [40] corroborated this and showed that with each increase of 20 cases annually, chances of receiving salvage therapy within 6 mo after RP is reduced with an OR of 0.92 (95% CI 0.88–0.98). The only study reporting on PCa-specific mortality by Bolton et al. [58] showed an increased risk for patients being treated by a low-volume (fewer than eight cases per year) versus a high-volume (eight or more cases per year) surgeon with a Fine-Gray subdistribution HR of 1.80 (95% CI 1.08–3.01).

3.3.2.2 Nononcological outcomes

3.3.2.2.1 Complications. Eight studies report on the association between annual surgical volume and overall intra- and postoperative complications. Seven out of the eight studies observed a significant reduction in complication rates with increasing surgical annual volume [40,41,53,56,57,59,63,67]. Of interest, Choi et al. [53] showed significantly fewer complications for high-volume surgeons than low- and intermediate-volume surgeons for ORP, whereas for MIRP, they reported similar complication rates, with the majority being respiratory complications. Finally, Vesey et al. [67] described an apparent reduction in postoperative complications for patients treated by surgeons with >15 cases annually. One study by Schmitges et al. [17] showed increased odds of perioperative rectal laceration for lower-volume surgeons (seven or fewer cases per year) with an OR of 3.26 (95% CI 1.93–5.51) compared with very-high-volume surgeons (≥51 cases per year). Two studies with contradicting results have been published regarding postoperative venous thromboembolisms as an outcome [16,54]. Another study by Sharma and Meeks [15] showed higher odds of open conversion during MIRP for low-volume surgeons with an OR of 7.38 (95% CI 4.47–12.17). Finally, three studies have reported higher transfusion rates for lower-volume surgeons [36,52,53], although for the study performed by Choi et al. [53], this was reported only for patients undergoing ORP and not for those undergoing MIRP. Furthermore, the study by Dash et al. [52] was published in 2004, and although not specifically mentioned, we suspect that most patients underwent ORP in this study.

3.3.2.2.2 Perioperative mortality. Four studies [18,45,59,66] reported on peri- and postoperative mortality, of which three studies [18,45,66] performed multivariable logistic regression analysis, showing a negative association between surgical volume and intra- and postoperative mortality. Both Hanchane et al. [45] and Walz et al. [66] reported a significant association between caseload volume and perioperative mortality, with ORs ranging from 0.1 to 0.32 between higher- and lower-volume surgeons, whilst Schmitges et al. [18] did not observe the same effect. They report OR values of 1.28 (95% CI 0.57–2.90) and 3.28 (95% CI 0.91–11.85) for low- versus intermediate-volume and low-versus high-volume surgeons, respectively, only hinting at lower mortality rates for higher-volume surgeons. As shown by Begg et al. [59], mortality rates after RP were low, with 60-d mortality rates ranging between 0.5% and 0.6%, which means that the studies were likely to be underpowered to detect differences in perioperative mortality.

3.3.2.2.3 Urinary incontinence. Two studies reported on postoperative urinary incontinence. Steinvik et al. [13] performed a multivariable analysis and could not find an association between surgeon volume and urinary incontinence defined as “use of pad(s) and/or moderate or severe urinary leaking problems”. Begg et al. [59] reported on “long-term incontinence” (>1 yr after surgery) and showed significantly lower rates of incontinence for very-high-volume surgeons (33–121 cases per year) with 16% of incontinence, compared with 19–20% for low-, medium-, and high-volume surgeons (<33 cases per year; p = 0.04).
one to 31 and ≤34 cases per year) and intermediate-volume (defined as 32–85 and 35–90 cases per year) centres have a higher chance of undergoing blood transfusion than those treated in high-volume centres (defined as >86 and >90 cases per year) [19,68]. Only one study by Schmitges et al. [19] performed a direct comparison of the transfusion rate of patients treated with ORP and MIRP (including both RARP and laparoscopic RP) in high-volume centres. They suggested that even for high-volume centres, the odds of needing blood transfusion is lower when treated by RARP, with an OR of 0.46 (95% CI 0.22–0.97) and 0.07 (95% CI 0.03–0.19) for homologous and autologous blood transfusion, respectively. In summary, except for blood transfusion, a largely similar impact of volume on all other outcomes was observed for patients treated with RARP and ORP.

3.3.4. **GRADE assessment**

A GRADE assessment was performed for outcomes with at least two included studies evaluating the same outcome. The results are summarised in Table 1. Overall, the certainty of evidence for oncological outcomes is very low or low for both studies investigating the impact of both hospital and surgeon caseload volumes. Evidence derived from retrospective observational studies is always expected to have a certain level of uncertainty; hence, the certainty is low at baseline for all included studies. Only for “need for additional therapies”, the level of certainty was upgraded to moderate, since the observed effect was strong, and a dose-response effect was observed. For similar reasons, the certainty of evidence for hospital volume and peri- and postoperative complications/death was upgraded to moderate as well.

### Table 1 – Summary of GRADE profiling of different reported outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Design</th>
<th>RoB</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other factors</th>
<th>Certainty</th>
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<td><strong>Hospital volume</strong></td>
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<td>Very low</td>
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<tr>
<td>BCR</td>
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<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None found</td>
<td>Very low</td>
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<td>Not serious</td>
<td>Not serious</td>
<td>None found</td>
<td>Very low</td>
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<tr>
<td>OS</td>
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<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None found</td>
<td>Very low</td>
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<tr>
<td>Complications</td>
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<td>Serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Strong effect, dose-response effect</td>
<td>Moderate</td>
</tr>
<tr>
<td>Open conversion</td>
<td>3</td>
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<td>Serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Strong effect, dose-response effect</td>
<td>Moderate</td>
</tr>
<tr>
<td>Blood transfusion</td>
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<td>Serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Strong effect, dose-response effect</td>
<td>Moderate</td>
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<tr>
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<td>Not serious</td>
<td>Not serious</td>
<td>Strong effect, dose-response effect</td>
<td>Moderate</td>
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<tr>
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<td>Not serious</td>
<td>Not serious</td>
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<td>Very low</td>
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<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Dose-response effect</td>
<td>Low</td>
</tr>
<tr>
<td>BCR</td>
<td>3</td>
<td>Observational</td>
<td>Serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Dose-response effect</td>
<td>Low</td>
</tr>
<tr>
<td>Need for additional therapy</td>
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<td>Serious</td>
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<td>Not serious</td>
<td>Not serious</td>
<td>Strong effect, dose-response effect</td>
<td>Moderate</td>
</tr>
<tr>
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<td>Observational</td>
<td>Serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
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<td>Blood transfusion</td>
<td>3</td>
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<td>Not serious</td>
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<td>Low</td>
</tr>
<tr>
<td>Peri- and postoperative mortality</td>
<td>4</td>
<td>Observational</td>
<td>Serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
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</tr>
<tr>
<td>Incontinence</td>
<td>2</td>
<td>Observational</td>
<td>Serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None found</td>
<td>Very low</td>
</tr>
</tbody>
</table>

BRC = biochemical recurrence; GRADE = Grading of Recommendations, Assessment, Development and Evaluations; OS = overall survival; PCSS = prostate cancer–specific survival; PSM = positive surgical margin; RoB = risk of bias.

3.4. **Discussion**

3.4.1. **Principal findings**

This review summarises the available evidence for the existence of a positive association between caseload volume and patient outcome for RP. Although all the included studies were retrospective observational studies with high RoB and confounding, for most outcomes the findings were consistent and demonstrated that a high caseload volume is associated with better oncological and nononcological outcomes.

Both higher hospital and surgeon caseload volumes were associated with a reduction in peri- and postoperative complication rates. Similarly, a higher hospital caseload volume was also strongly associated with a reduction in open conversion for MIRP and a reduction in blood transfusion rates. Studies investigating surgeon caseload volume generally did not correct for hospital characteristics in a multivariable analysis. However, high-volume surgeons are more likely to work in high-volume centres, which itself provides a partial implicit correction for the level of expertise of the hospital. The one study that corrected for both clustering and case mix showed a mild reduction in postoperative complications only for highest-volume surgeons performing 33–121 cases per year [59]. Furthermore, a “field effect” appeared to exist for lower-volume surgeons working in high-volume hospitals, leading to better results for lower-volume surgeons. This effect has previously been described for surgeons performing pancreaticoduodenectomies [69]. It is generally believed that a hospital’s annual caseload is a surrogate measurement for structural and...
standardised process components that are followed at high-volume hospitals, leading to fewer medical errors being made, higher quality of perioperative care, and hence a reduction in complication rates and mortality [70]. Gilbert et al. [47] suggested a similar finding with the effect of hospital volume on mortality vanishing after the adjustment for the number of other uro-oncological surgeries (as a surrogate for experience in cancer surgery), suggesting that the infrastructure plays a determining role.

There were very limited data on the association of surgeon/hospital volume with urinary continence and erectile function. For erectile function, only one study was eligible for inclusion and it showed significantly higher rates of potency at 6-yr follow-up with increasing hospital annual caseload, especially for the highest-volume hospitals with >200 cases per year [60]. For urinary continence, the existing data were contradictory with studies being equally split between those showing any association and those showing no association between surgeon/hospital caseload volume and long-term continence rates. It is important to note that erectile function and continence are determined by variable operative-, patient-, and disease-related factors [6,71,72]. Therefore, surgical or hospital annual volume may be considered less as a direct factor, leading to better continence and potency outcomes. However, data remain very limited, and heterogeneous definitions of potency and incontinence remain a known issue when interpreting retrospective data.

For oncological outcomes, there is an association between a higher annual hospital volume and a reduction in PSM. This association was not as strong for surgical volume as for hospital volume. This is probably due to the fact that this systematic review included only studies reporting annual caseload; studies looking at the learning curve or previous relevant experience of individual surgeons were excluded. These factors also play an important role in the quality of the surgery, together with the variation between individual surgeons even amongst high-volume surgeons [73]. The use of adjuvant or salvage therapies was clearly associated with surgeon caseload volume, which can be expected if more PSMs occur. Although we cannot completely exclude the possibility that the observed effect was due to nonadherence to guidelines, this seems less plausible since a plethora of evidence exists across all types of cancer demonstrating that guidelines adherence rates improve with increasing hospital volume [74–78]. Hence, we expect this effect to be a direct result of the quality of cancer care. Data on other long-term oncological outcomes were too limited to draw any conclusions. Although it is not a hard endpoint, the use of adjuvant/salvage therapies is highly relevant because it is associated with more therapy-related toxicity, which might be prevented if treated by a higher-volume surgeon [79].

Although the available data comparing RARP and ORP were limited, overall, the impact of hospital volume on peri- and postoperative complications seems to be independent of the surgical technique. This does not exclude the possibility that the absolute complication rates might be different between both approaches, but it suggests that for both approaches, the role of hospital volume is similar.

Secondly, as expected, the need for transfusion appeared to be higher in ORP than in minimally invasive techniques. Probably because the need for blood transfusion was lower when treated with RARP, only patients treated in the highest-volume centres have lower odds of receiving blood transfusion than those in low-volume centres. Based on these data, no recommendations can be given on which surgical technique is safer for both oncological and nononcological outcomes, but it demonstrates the impact of high-volume centres for both ORP and RARP.

With the existing data, it is difficult to define a minimal annual caseload cut-off that is needed to achieve the highest quality of care for PCa patients. This is especially true for surgeon volume, since an inherently skillful low-volume surgeon might have equal or better outcomes than a less skillful higher-volume surgeon. For hospital volume, this is somewhat different, because it is rather a reflection of hospital quality and standardisation of the procedure. A less experienced surgeon can profit from the standardisation and experience of the whole team, leading to better outcomes when compared with a low-volume hospital. Hospital volume is therefore probably less influenced by individual surgeon factors such as learning curve and innate skill.

In order to provide an estimation at which annual caseload patient outcomes start to clearly improve, the median annual hospital caseload was calculated based on the lower threshold at which the ORs and the accompanying 95% CIs presented in the forest plots completely cross 1. Based on these data, a minimum hospital caseload volume threshold that results in clearly better outcomes was estimated to be 86 (IQR 35–100) cases per year. This threshold is similar to the annual minimum caseload thresholds that are already being used in the Netherlands (>100 cases per year) and the UK (>150 cases per year), which are based on cost-effectiveness analyses [80,81]. Although centralisation of care based on a certain volume cut-off could theoretically reduce mortality and PSMs, logistically it may not be feasible in all countries. The workload at high-volume hospitals might become too high, leading to increased waiting times and possibly reduced quality of care [82]. Furthermore, annual hospital caseload will always remain a surrogate for quality of care, which is influenced not only by surgical numbers, but also by the quality of the whole care team (imaging, treatment choices made, peri- and postoperative care, quality of follow-up, etc.). It is not impossible for low-volume centres to achieve similar (or potentially better) outcomes to high-volume centres, but it probably requires much more effort of the whole infrastructure to reach this goal.

Based on our findings presented, we do not advocate defining a stringent cut-off that defines a high-volume centre. Volume thresholds need to be combined with prospective patient selection and outcome measurements for benchmarking purposes and to make centres’ outcomes publicly available for patients. This allows for a critical appraisal of a centre’s performance, which has been shown to lead to improved patient care [83,84].
3.4.2. Strengths and limitations

One of the main strengths of this systematic review is that it has been developed and conducted by a multidisciplinary panel of experts (EAU Prostate Cancer Guidelines Panel) supported by a strong methodology team (EAU Guidelines Office Methods Committee). The review has been performed robustly in accordance with recognised standards. This has led to the most up-to-date and most methodologically sound systematic review that has been published on this topic.

Limitations include the nature of included studies, which were all retrospective observational studies, resulting in high RoB and confounding, and clinical and methodological heterogeneity across studies. This strong heterogeneity and poor reporting of patient characteristics did not allow for a sensitivity analysis. With different high- versus low-volume definitions that were used and poor reporting on patient characteristics, data interpretation and evidence synthesis were challenging. GRADE profiling highlighted the fact that the quality of the evidence for (1) hospital volume was very low for oncological outcomes and incontinence, and (2) surgeon volume was low to very low for all outcomes, except for the need for additional therapy. This means that for these outcomes, the true effect may clearly be different from what we have observed in this review. For hospital volume, the quality of evidence for the nononcological outcomes was upgraded to moderate due to the observed strong dose-response effect. This means that the observed effect is likely to be close to the true effect. This is true as well for surgeon volume and the need for additional therapy. However, due to the retrospective nature of the included studies, we must remain cautious in drawing strong conclusions from these data.

4. Conclusions

Higher hospital volume for RP, defined as annual caseload, is associated with fewer perioperative complications and lower rates of PSMs. A higher surgeon volume is associated with less need for additional therapies and lower rates of PSMs and complications. This association becomes apparent for a hospital caseload of between 35 and 100 (median 86) cases per year. Owing to the remaining uncertainty of the summarised evidence, it remains impossible to impose a minimum annual caseload that needs to be achieved. However, this review shows significant differences in both oncological and nononcological outcomes between high- and low-volume centres; hence, both high- and low-volume centres are encouraged to measure their outcomes, make them publicly available, and further improve their quality of care if needed.

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Appendix A. Supplementary data

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References


