

Robotic vs. Retropubic radical prostatectomy in prostate cancer: A systematic review and a meta-analysis update

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ABSTRACT

CONTEXT: The safety and feasibility of robotic-assisted radical prostatectomy (RARP) compared with retropubic radical prostatectomy (RRP) is debated. Recently, a number of large-scale and high-quality studies have been conducted.

OBJECTIVE: To obtain a more valid assessment, we update the meta-analysis of RARP compared with RRP to assess its safety and feasibility in treatment of prostate cancer.

METHODS: A systematic search of Medline, Embase, Pubmed, and the Cochrane Library was performed to identify studies that compared RARP with RRP. Outcomes of interest included perioperative, pathologic variables and complications.

RESULTS: 78 studies assessing RARP vs. RRP were included for meta-analysis. Although patients underwent RRP have shorter operative time than RARP (WMD: 39.85 minutes; $P < 0.001$), patients underwent RARP have less intraoperative blood loss (WMD = -507.67ml; $P < 0.001$), lower blood transfusion rates (OR = 0.13; $P < 0.001$), shorter time to remove catheter (WMD = -3.04day; $P < 0.001$), shorter hospital stay (WMD = -1.62day; $P < 0.001$), lower PSM rates (OR:0.88; $P = 0.04$), fewer positive lymph nodes (OR:0.45; $P < 0.001$), fewer overall complications (OR:0.43; $P < 0.001$), higher 3- and 12-mo potent recovery rate (OR:3.19; $P = 0.02$; OR:2.37; $P = 0.005$, respectively), and lower readmission rate (OR:0.70, $P = 0.03$). The biochemical recurrence free survival of RARP is better than RRP (OR:1.33, $P = 0.04$). All the other calculated results are similar between the two groups.

CONCLUSIONS: Our results indicate that RARP appears to be safe and effective to its counterpart RRP in selected patients.

INTRODUCTION

Prostate cancer (PCa) is the most common cancer in the worldwide and its morbidity, mortality is the first and second common cancer in men, respectively [1]. RP is the standard therapy for patients with localized PCa [2]. However, open retropubic radical prostatectomy (RRP) is associated with higher overall complications, including estimated blood loss (EBL), wound infections. With the development of surgical techniques, laparoscopic

techniques and robot assisted surgeries have become a very popular procedure for the management of urological disease throughout the world [3]. Compared with RRP, the advantages of laparoscopic radical prostatectomy (LRP) are less EBL, fewer complications, better cosmetic effect and shorter hospital stay [4]. The disadvantages of LRP is lack of 3D visualization and poor ergonomics.

As alternatives to open surgery, RARP has become a predominant procedure for the treatment the localized prostate cancer in the world [5]. Assessing of the robotic

Table 1: Characteristics of included studies

First author, year	Country	Study interval	Design	LOE	No.of patients RARP/RRP	Matching/ comparable*	Quality score ^A
Ahlering, 2004	USA	2001-2002	Prospective	3b	60/60	1, 2, 3, 4	*****
Bae, 2012	Korea	2008-2011	Retrospective	3b	111/70	1, 2, 3, 4, 5, 6	*****
Ball, 2006	USA	2000-2005	Prospective	3b	82/135	1, 3, 5, 6	*****
Barocas, 2010	USA	2003-2008	Prospective	3b	1413/491	1, 3, 7	*****
Bolenz, 2010	USA	2003-2008	Retrospective	3b	262/161	1, 2, 3, 4, 6	*****
Breyer, 2010	USA	2002-2008	Prospective	3b	293/695	1, 3, 4, 5, 6, 7	*****
Carlsson, 2010	Sweden	2002-2007	Prospective	3b	1253/485	1, 3, 4, 5,	*****
Chan, 2008	USA	2003-2006	Retrospective	3b	660/340	1, 3, 5, 6	*****
Chino, 2009	USA	2003-2007	Retrospective	3b	368/536	1, 3, 5, 6	*****
Choi, 2012	Korea	2007-2011	Retrospective	3b	354/247	1, 3, 5	****
Choo, 2013	Korea	2003-2010	Prospective	3b	77/176	1, 2, 3, 4, 5, 6, 7	*****
Chung, 2012	Taiwan	2006-2009	Retrospective	4	274/1773	1, 7	****
D'Alonzo, 2009	USA	2003-2006	Retrospective	3b	256/280	1, 2, 3, 4, 7	*****
Di Pierro, 2011	Switzerland	2007-2009	Prospective	3b	75/75	1, 3, 5, 6, 7	*****
Doumerc, 2010	France	2006-2008	Prospective	3b	212/502	1, 3, 4, 5, 6, 7	*****
Drouin, 2009	France	2000-2004	Retrospective	3b	71/83	1, 2, 3, 5, 6, 7	*****
Farnham, 2006	USA	2003-2004	Prospective	3b	176/103	1, 3, 4, 6	*****
Ficarra, 2009	Italy	2006-2007	Prospective	3b	103/105	1, 2, 3, 4, 5, 6, 7	*****
Fracalanza, 2008	Italy	2006	Prospective	3b	35/26	1, 2, 3, 4, 6	*****
Forehner, 2013	Germany	2007-2011	Prospective	3b	252/1925	1, 3, 6, 7	*****
Hong, 2010	Korea	2007	Retrospective	4	26/25	1, 2, 7	****
Park, 2014	Korea	2007-2012	Retrospective	3b	730/277	1, 2, 3, 4, 5, 6, 7	*****
Busch, 2015	Germany	NA	Prospective	3b	194/194	1, 3, 5, 6	*****
Kim, 2011	Korea	2007-2010	Prospective	3b	528/235	1, 2, 3, 5, 6, 7	*****
Kordan, 2010	USA	2003-2006	Prospective	3b	830/414	1, 2, 3, 5, 6	*****
Krambeck, 2008	USA	2002-2005	Prospective	3b	294/588	1, 2, 3, 5, 6, 7	*****
Laurila, 2009	USA	2006	Retrospective	3b	94/98	1, 3, 5, 6	*****
Lo, 2010	HongKong	2006-2007	Retrospective	3b	20/20	1, 3, 5, 6, 7	*****
Magheli, 2011	USA	2000-2008	Prospective	3b	522/522	1, 3, 4, 5, 6, 7	*****
Malcolm, 2010	USA	2000-2008	Retrospective	3b	477/135	1, 3, 5, 6, 7	*****
Menon, 2002	France	2001	Prospective	3b	30/30	1, 3, 4, 5, 6, 7	*****
Miller, 2007	USA	2002-2006	Prospective	4	42/120	1	****
Minniti, 2011	Italy	2007-2008	Prospective	3b	22/93	1, 2, 3, 5	****
Nelson, 2007	USA	2003-2006	Prospective	3b	629/374	1, 3, 6	*****
OU, 2009	Taiwan	2004-2007	Retrospective	3b	30/30	1, 2, 3, 4, 5, 6	*****
Pilecki, 2014	USA	2011	Retrospective	4	4374/1097	1, 2	****
Rocco, 2009	Italy	2004-2007	Prospective	3b	120/240	1, 3, 5, 6, 7	*****
Ryu, 2013	Korea	2007-2012	Prospective	4	524/341	1, 2, 3, 4	*****
Schroeck, 2008	USA	2003-2007	Retrospective	3b	362/435	1, 2, 3, 4, 5, 6, 7	*****
Shapiro, 2014	USA	2000-2010	Retrospective	3b	108/229	1, 3, 5, 6, 7	*****
Silberstein, 2012	USA	2010	Retrospective	4	126/126	1, 3, 5, 6	*****
Smith, 2007	USA	2002-2006	Retrospective	3b	200/200	1, 2, 3, 4, 5, 6	*****
Son, 2013	Korea	2006-2009	Retrospective	3b	146/112	1, 2, 3, 4, 6, 7	*****
Stranne, 2010	Sweden	2002-2006	Retrospective	3b	946/465	1, 2, 3, 4, 5, 6, 7	*****
Sugihara, 2014	Japan	2012-2013	Retrospective	3b	2126/7202	1, 2, 5,	****
Tewari, 2003	USA	1999-2002	Prospective	3b	200/100	1, 2, 3, 4, 5, 6, 7	*****
Truesdale, 2010	USA	2005-2009	Retrospective	3b	99/217	1, 2, 3, 5, 6	*****
Vora, 2013	USA	1997-2010	Retrospective	3b	140/95	1, 3, 5, 6, 7	*****

White, 2009	USA	2005-2008	Retrospective	3b	50/50	1, 3, 5, 6	*****
Williams, 2010	USA	2005-2008	Retrospective	4	604/346	1, 3, 5, 6	*****
Wood, 2007	USA	2003-2005	Prospective	4	165/152	1, 3, 7	*****
Yi, 2010	Korea	2006-2009	Retrospective	3b	153/641	1, 2, 3, 6, 7	*****
Rush, 2015	Canada	2009-2012	Retrospective	3b	331/643	1, 2, 3, 4, 7	*****
Ong, 2015	Australian	2009-2012	Prospective	3b	885/1117	1, 3, 5, 6, 7	*****
Porcaro, 2015	Italy	2013	Retrospective	4	108/43	1, 2, 3, 4, 5, 6, 7	*****
O'Neil, 2015	USA	2011-2012	Prospective	3b	933/1505	1, 3, 6, 7	****
Niklas, 2015	Germany	2003-2010	Retrospective	3b	932/499	1, 2, 3, 4, 5, 6, 7	*****
Haglund, 2015	Sweden	2008-2011	Prospective	3b	1847/778	1, 2, 3, 5, 6	*****
Gagnon, 2014	Canada	NA	Retrospective	3b	200/200	1, 2, 3, 4, 5, 6, 7	*****
Davison, 2014	Canada	2007-2009	Prospective	3b	78/73	1, 3, 5	*****
Akand, 2015	Turkey	1999-2012	Retrospective	4	79/50	1, 2, 3, 4, 5, 7	*****
Korets, 2014	USA	2007-2012	Retrospective	3b	12746/3398	1, 2, 7	*****
Wallerstedt, 2015	Sweden	NA	Prospective	3b	1847/778	1, 2, 3, 5, 6, 7	*****
Hu, 2015	USA	2004-2009	Retrospective	3b	5524/7878	1, 2, 3, 5, 6, 7	*****
Davis, 2014	USA	2004-2010	Prospective	3b	27348/13840	1, 7	****
Rithch, 2014	USA	2003-2009	Retrospective	3b	742/237	1, 2, 3, 5, 6, 7	*****
Gandaglia, 2014	USA	2008-2009	Retrospective	3b	3476/2439	1, 3, 5, 6, 7	*****
Koo, 2014	Korea	1992-2008	Retrospective	3b	175/175	1, 3, 5, 6, 7	*****
Busch, 2014	Germany	NA	Retrospective	3b	110/110	1, 2, 3, 4, 5, 6, 7	*****
Alemozaffar, 2015	USA	2000-2010	Prospective	3b	282/621	1, 2, 3, 4, 5, 6, 7	*****
Harty, 2013	USA	2000-2010	Prospective	3b	152/153	1, 3, 4, 5, 6, 7	*****
Silberstein, 2013	USA	2007-2010	Retrospective	3b	493/961	1, 3, 5, 7	*****
Ludovico, 2013	Italy	2004-2008	Retrospective	3b	82/48	1, 3, 5, 6, 7	*****
Musch, 2013	Germany	2009-2010	Retrospective	3b	105/105	1, 2, 3, 4, 5, 6, 7	*****
Hall, 2014	Australia	2007-2009	Retrospective	3b	100/100	1, 3, 6	*****
Geraerts, 2013	Belgium	2009-2011	Prospective	3b	64/116	1, 2, 7	*****
Drouin, 2014	France	2007-2010	Prospective	3b	73/44	1, 3, 5, 6, 7	*****
Pierorazio, 2013	USA	2002-2011	Retrospective	3b	105/743	1, 2, 3, 4, 5, 6, 7	*****

RARP=robot-assisted radical prostatectomy; RRP= retropubic radical prostatectomy; NA= data not available; LOE= level of evidence.

*:Matching/comparable variable: 1=age, 2=BMI, 3=PSA, 4=prostate size, 5=clinical stage, 6= biospy Gleason score, 7=follow up

Δ:based on Newcastle-Ottawa Scale.

surgery by expert indicate better ergonomics and quicker learning curve, but its shortage is high cost of the robotic surgery system.

In recent years, many experts have reported on comparative study of RARP and open RRP. And some meta-analysis were performed to evaluate the advantages and disadvantages of two approaches, including perioperative outcomes, oncologic outcomes [5]. Their early experience showed that the outcomes of this approach with fewer overall complications, quicker convalescence, and lower EBL and transfusion [5-7]. However, the outcomes of RARP compared with RRP have not been fully evaluated, and no conclusive results are available. Therefore, a systematic review and meta-analysis of the included published studies was performed to compare RARP with RRP.

RESULTS

Characteristics of eligible studies

According to search strategy, the included 78 studies[4, 8-85] assessing RARP vs. RRP met the inclusion criteria and were applied to perform this meta-analysis (Figure 1). Those studies include forty-three retrospective and thirty-five prospective studies and were listed in Table 1.

Quality of the studies and level of evidence (Table 1)

In this meat-analysis, the Newcastle-Ottawa Scale quality assessment method of the observational studies [86], and the US Preventive Services Task Force grading system [87] were applied to evaluate the quality of included studies. Twenty studies scored seven stars and

Table 2: Overall analysis of demographic and clinical characteristics compared RARP with RRP

Outcomes of interest	No. of studies	No. of patients RARP/RRP	OR/WMD(95% CI)	p-value	Study heterogeneity			
					Chi ²	df	I ²	p-value
Age(year)	33	41866/227181	-1.00[-1.56,-0.44]	<0.001	1260.51	32	97%	<0.001
BMI(kg/m ²)	17	9365/4690	-0.10[-0.39,0.20]	0.52	87.93	16	82%	<0.001
Pre-PSA(ng/ml)	23	6161/5250	-0.93[-1.47,-0.40]	<0.001	234.69	22	91%	<0.001
Prostate volume(ml)	12	3995/3288	2.35[-0.92,5.61]	0.16	136.49	11	92%	<0.001

RARP=robot-assisted radical prostatectomy; RRP=retropubic radical prostatectomy; OR = odds ratio; WMD = weighted mean difference; CI = confidence interval; BMI = body mass index.

were evaluated as the high quality studies. Additionally, The clinical variables of RARP and RRP were extracted independently from included literatures (Table 1).

Description of included studies and patients Demographics (Table 2)

Patients underwent RARP are younger (WMD = -1.00 years; 95% CI: -1.56 to -0.44; *P* < 0.001) (Figure S1), and have the lower level of pre-PSA (OR = -0.93; 95% CI: -1.47 to -0.40; *P* < 0.001) (Figure S2). But there is no significant difference on BMI (OR = -0.10; 95% CI: -0.39 to 0.20; *P* = 0.20) (Figure S3), and prostate volume (WMD = 2.35ml; 95% CI: -0.92 to 5.61; *P* = 0.16) (Figure S4) between the RARP and RRP group. (Table 2).

Outcomes of perioperative variables (Table 3)

Operating time and estimated blood loss (EBL)

With respect to perioperative variables, pooling data of 18 studies [21, 23, 24, 26, 29, 32, 34, 40, 54, 59, 60,

64, 70, 75, 78, 81, 84, 85] involving 54261 participants indicated that RARP has longer operative time than RRP (WMD: 39.85 minutes; 95% CI: 20.95 to 58.75; *P* < 0.001) (Figure 2). Pooling data of 13 studies [10, 21, 23, 29, 30, 34, 40, 60, 70, 75, 78, 84, 85] results showed that RARP has less intraoperative blood loss (WMD = -507.67ml; 95% CI: -633.21 to -382.12; *P* < 0.001) (Figure 3).

Transfusion rate and postoperative recovery

Pooled data from the 26 studies [9, 10, 14, 21, 23, 24, 26, 29, 30, 34, 35, 40, 44-46, 54, 59, 64, 72, 73, 78, 80, 82, 84] reported transfusion rate between RARP and RRP, and the results showed that RARP was associated with lower transfusion rate (OR = 0.13; 95% CI: 0.08 to 0.21; *P* < 0.001) than RRP (Figure 4). Pooling data of 5 studies reported on the time to remove catheter, the forest plot showed that RARP had shorter time to remove catheter than RRP group (WMD = -3.04; 95% CI: -4.59 to -1.49; *P* < 0.001) (Figure S5). And pooling date of 11 studies [10, 23, 24, 34, 53, 54, 64, 75, 78] reported on length of hospital stay (LOS), the forest plot showed that RARP had a shorter LOS than RRP (WMD = -1.62; 95% CI: -2.42 to -0.82; *P* < 0.001) (Figure 5).

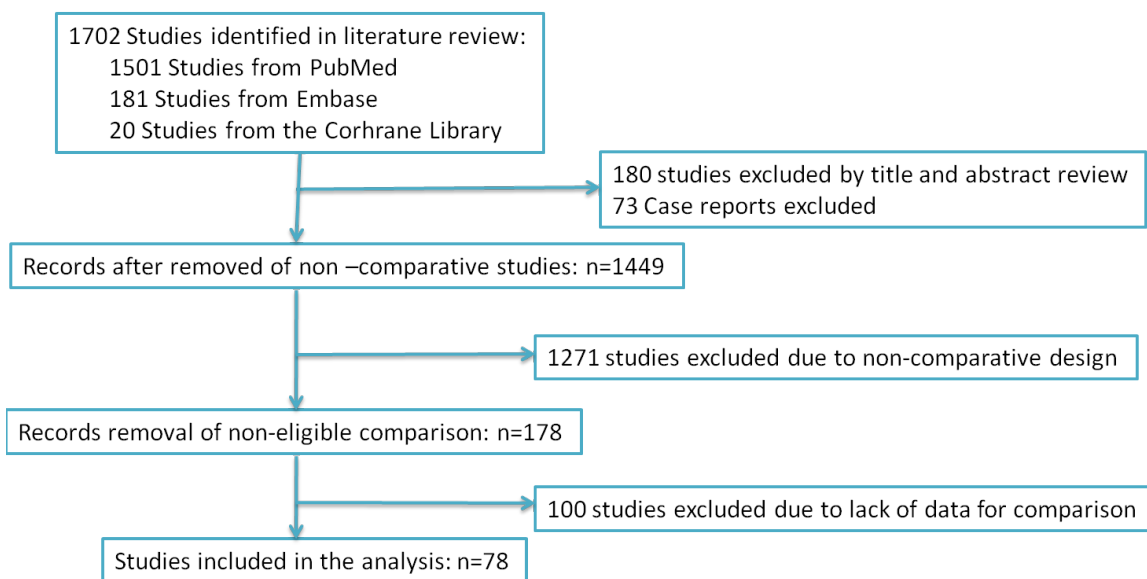


Figure 1: PRISMA diagram. The search strategy and number of studies identified for inclusion in this meta-analysis.

Table 3: Overall analysis of perioperative outcomes comparing RARP with RRP

Outcome of interest	No. of studies	No. of patients RARP/RRP	OR/WMD(95%CI) †	p-value	Study heterogeneity			
					Chi²	df	I²	p-value
Operation time, min	18	36296/17965	39.85[20.95,58.75] †	<0.001	2130.01	17	99%	<0.001
Estimated blood loss, ml	13	3446/2791	-507.67[-633.21,-382.12] †	<0.001	390.34	12	97%	<0.001
Transfusion rate	26	54847/32967	0.13[0.08,0.21]	<0.001	693.85	25	96%	<0.001
Remove the catheter, day	5	2135/1264	-3.04[-4.59,-1.49] †	<0.001	260.52	4	98%	<0.001
Hospital stay, day	11	32196/17106	-1.62[-2.42,-0.82] †	<0.001	1517.19	10	99%	<0.001

RARP=robot-assisted radical prostatectomy; RRP=retropubic radical prostatectomy; OR = odds ratio; WMD = weighted mean difference; CI = confidence interval.

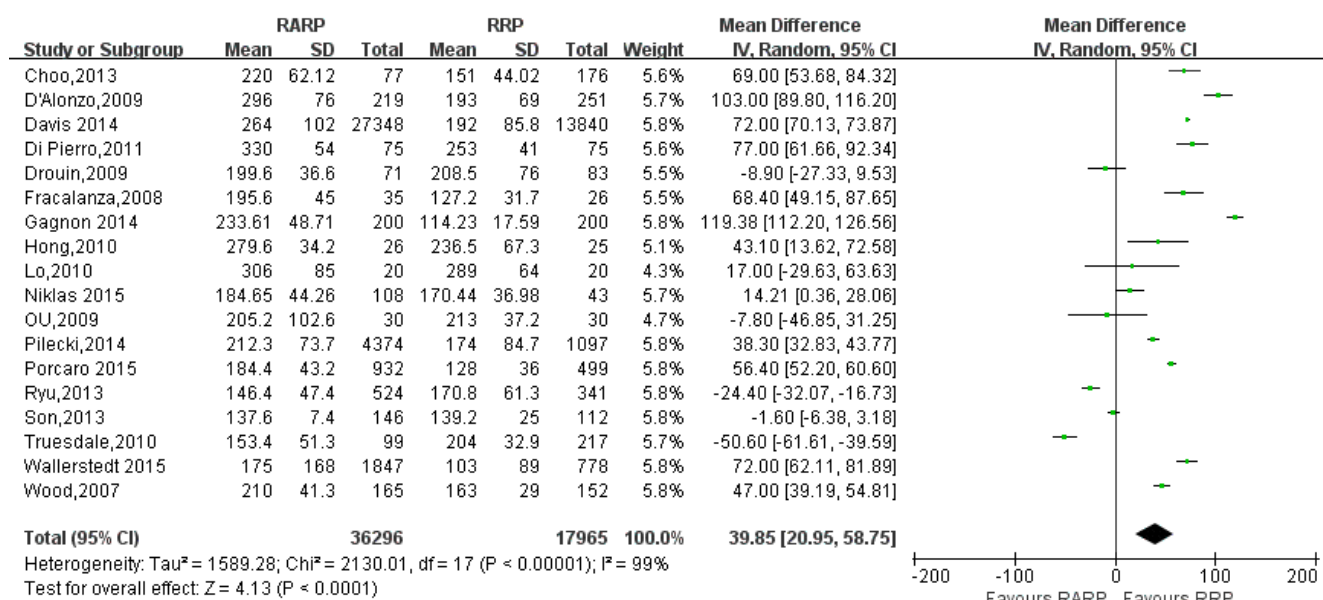


Figure 2: Forest plot and meta-analysis of operating time between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

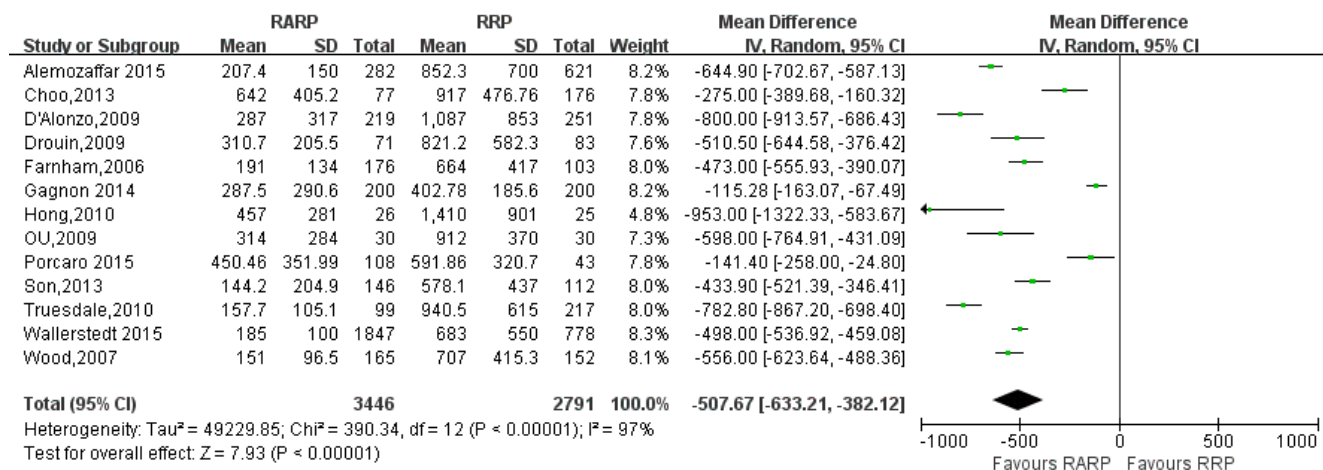


Figure 3: Forest plot and meta-analysis of estimated blood loss between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

Outcomes of oncological variables

pathologic stage and pathologic Gleason score (Table 5)

14 studies [9, 20, 27-29, 32, 46, 48, 66, 70, 73, 76,

77, 80] on $\leq pT2a$, $pT2b$, $\geq pT2c$, 48 studies [8-13, 15, 16, 18, 19, 21, 26-29, 31, 32, 34, 42-44, 46-50, 52, 54, 55, 57, 58, 60, 61, 64-71, 73, 74, 76-78, 82, 85] on pathologic Gleason score (≤ 6 ; 7 ; ≥ 8) were reported, respectively. The results showed a statistical differences more Gleason score

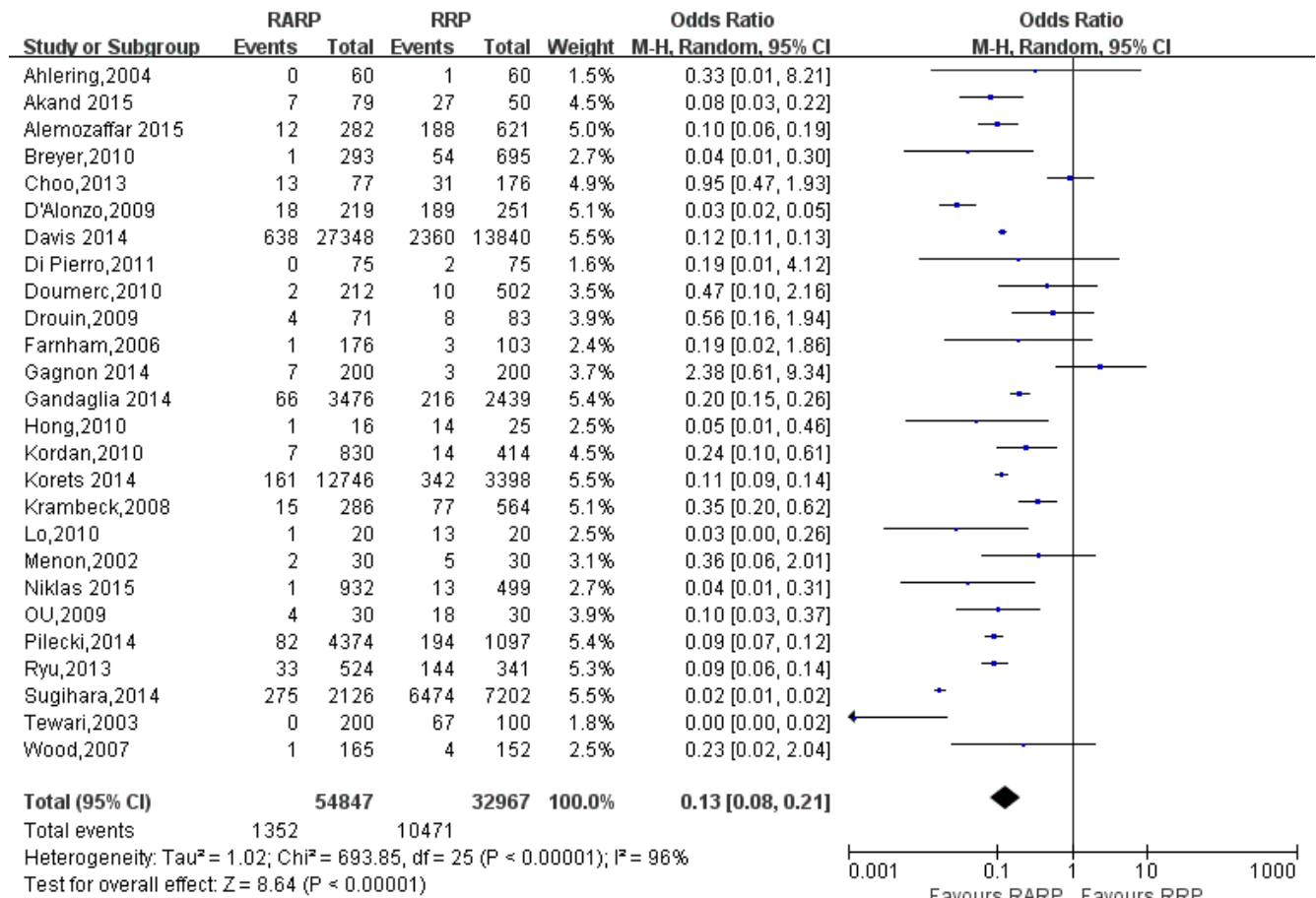


Figure 4: Forest plot and meta-analysis of transfusion rate between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

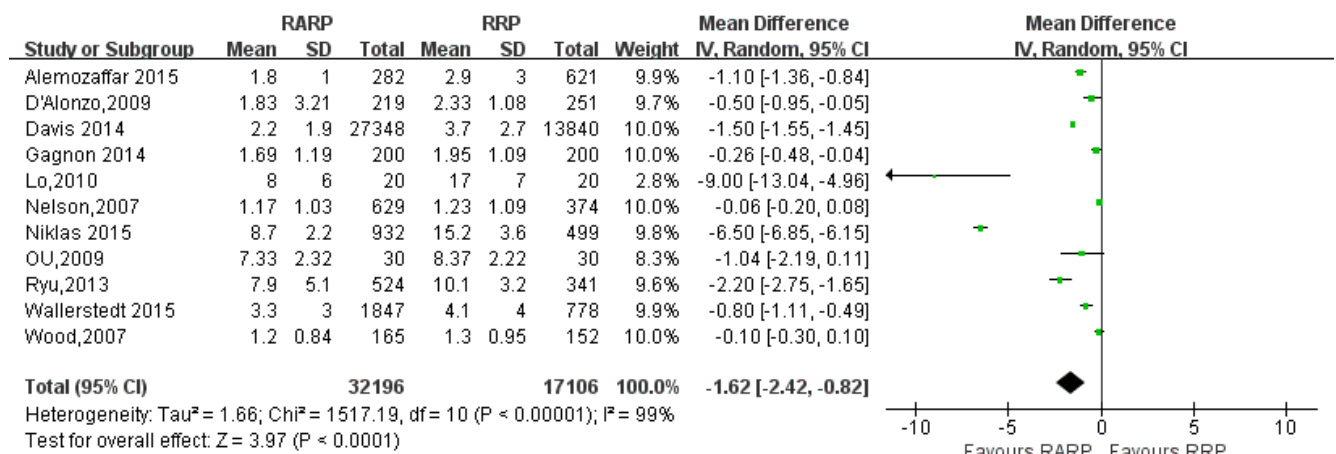


Figure 5: Forest plot and meta-analysis of the length of hospital stay between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

Table 4: Overall analysis of complications comparing RARP and RRP

Outcome of interest	No. of studies	No. of patients RARP/RRP	OR (95%CI)	p-value	Study heterogeneity			
					Chi ²	df	I ²	p-value
Overall complications	25	43087/28834	0.43 [0.32, 0.58]	<0.001	499.59	24	95%	<0.001
Rectal injury	8	3888/8110	0.16[0.07, 0.39]	<0.001	5.22	7	0%	0.63
Pulmonary embolism	9	37575/24635	0.47[0.37, 0.59]	<0.001	5.04	8	0%	0.75
Wound infections	10	11161/10587	0.23[0.11, 0.46]	<0.001	31.49	9	71%	<0.001
Bladder neck contracture	4	1993/2409	0.21[0.08,0.60]	0.003	8.39	3	64%	0.04
UTI	4	6586/2546	0.75[0.37,1.54]	0.44	15.35	3	80%	0.002
Urinary retention	3	2042/960	0.63[0.47,0.84]	0.002	2.44	2	18%	0.29
Obturator nerve injury	2	1453/585	0.09[0.01,0.75]	0.03	0.01	1	0%	0.91
DVT	7	7479/3072	0.40[0.25,0.66]	<0.001	10.82	6	45%	0.09
Urinary leakage	8	30940/15631	0.64[0.58,0.70]	<0.001	8.87	7	21%	0.26
ileus	8	3412/8501	0.92[0.56,1.51]	0.73	2.20	7	0%	0.95
lymphocele	9	45258/2639	0.52[0.29,0.94]	0.03	8.93	8	10%	0.35
Urinary continence-3mo	9	997/941	1.54[0.92,2.58]	0.10	22.06	8	64%	0.005
Urinary continence-12mo	9	1565/2179	1.03[0.84,1.27]	0.75	17.41	8	54%	0.03
Potent recovery-3mo	5	1169/820	3.19[1.19,8.56]	0.02	51.94	4	92%	<0.001
Potent recovery-12mo	7	1395/1574	2.37[1.30,4.33]	0.005	55.43	6	89%	<0.001
Readmission rate	7	11632/7060	0.83[0.74,0.94]	0.002	36.82	6	84%	<0.001

RARP=robot-assisted radical prostatectomy; RRP=retropubic radical prostatectomy; OR = odds ratio; WMD = weighted mean difference; CI = confidence interval; UTI=urinary tract infection; DVT=deep venous thrombosis.

Table 5: Overall analysis of pathologic and oncological outcomes comparing RARP with RRP

Outcome of interest	No. of studies	No. of patients RARP/RRP	OR/WMD(95%CI)	p-value	Study heterogeneity			
					Chi ²	df	I ²	p-value
Pathologic T stage								
≤pT2a	13	2147/2174	1.11[0.93,1.31]	0.26	8.84	12	0%	0.72
pT2b	11	1959/2098	1.11[0.93,1.33]	0.25	13.91	10	28%	0.18
≥pT2c	14	2268/2485	0.93[0.76,1.13]	0.44	11.19	13	0%	0.60
Pathological Gleason score								
≤6	48	15238/13412	1.04[0.91,1.18]	0.61	224.21	47	79%	<0.001
7	48	15238/13412	1.17[1.04,1.33]	0.01	230.23	47	80%	<0.001
≥8	48	15238/13412	0.68[0.60,0.78]	<0.001	101.358	47	54%	<0.001
PSM	49	20804/23133	0.88[0.78,1.00]	0.04	198.74	48	76%	<0.001
PSM for T2	28	10086/9711	0.77[0.63,0.95]	0.01	82.23	27	67%	<0.001
PSM for T3	18	2011/2125	1.46[1.27,1.67]	<0.001	18.66	17	9%	0.35
Mean lymph node yield	4	837/565	2.85[-0.92,6.63] [†]	0.14	115.32	3	97%	<0.001
Positive lymph node	16	4162/6500	0.45[0.31,0.65]	<0.001	32.02	15	53%	0.006
BCR for free survival	10	4342/4176	1.33[1.01,1.76]	0.04	39.04	9	77%	<0.001

RARP=robot-assisted radical prostatectomy; RRP=retropubic radical prostatectomy; OR = odds ratio; WMD = weighted mean difference; CI = confidence interval; PSM=positive surgical margins; [†]value of WMD.

= 7 (OR: 1.17; 95% CI: 1.04 to 1.33; P = 0.01; Figure 6) performed RARP and more Gleason score ≥8 (OR: 0.68; 95% CI: 0.60 to 0.78; P < 0.001; Figure 6) in RRP. However, there were no statistical differences with respect to Gleason score ≤6 (OR: 1.04; 95% CI: 0.91 to 1.18; P = 0.61; Figure 6) and pathologic T stage in the two groups (Figure S6,7,8)(Table 5).

Positive surgical margins and lymph node yield (Table 5)

49 studies [9-12, 14-16, 18, 19, 21, 26-29, 31-34, 36, 37, 39, 41-44, 46-49, 52, 54, 56-58, 61, 62, 65, 67-69, 73, 76-78, 80-82, 84] evaluating RARP and RRP reported positive surgical margins(PSM) rates. The results showed a significant difference with higher PSM rates in RRP group (OR:0.88; 95% CI: 0.78 to 1.00; P =

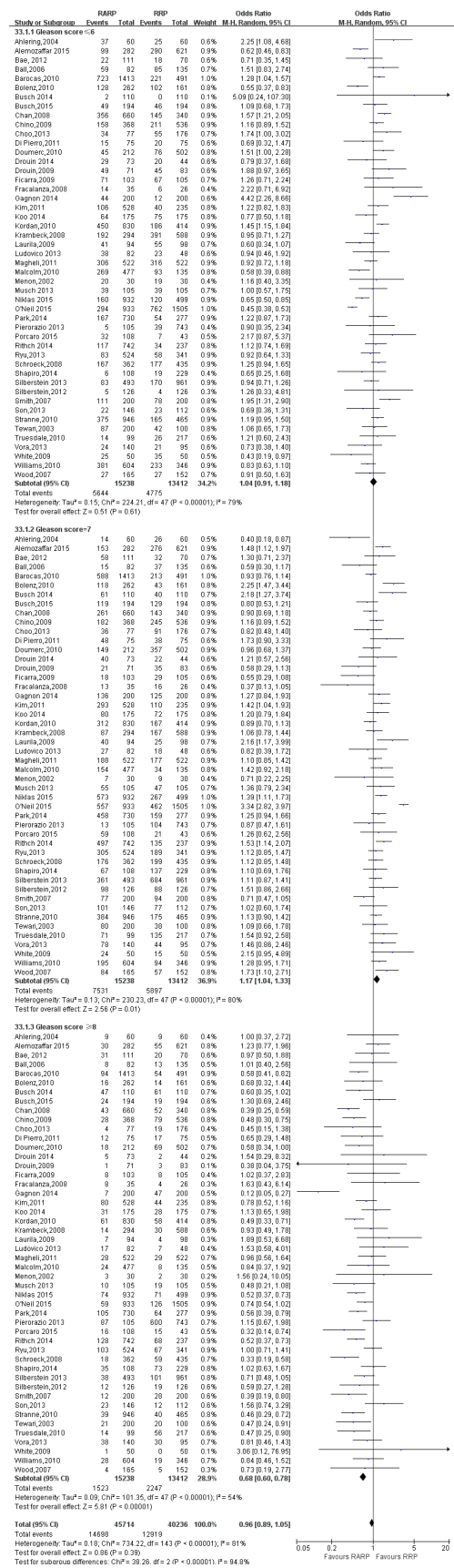


Figure 6: Forest plot and meta-analysis of pathological Gleason Score between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retrorectal radical prostatectomy.

Table 6: Sensitivity analysis of high quality studies comparing RARP with RRP

Outcome of interest	No. of studies	No. of patients RARP/RRP	OR/WMD(95%CI) †	p-value	Study heterogeneity			
					Chi²	df	I²	p-value
Operation time, min	10	1523/1435	44.43[8.01,80.84] †	0.02	1166.56	9	99%	<0.0001
Estimated blood loss, ml	8	1080/1102	-493.41[-672.09,-314.74] †	<0.001	217.36	7	97%	<0.0001
Transfusion rate	18	16249/7209	0.16[0.09,0.28]	<0.001	116.44	17	85%	<0.0001
Remove the catheter, day	3	1173/735	-1.78[-2.50,-1.06] †	<0.001	19.52	2	90%	<0.0001
Hospital stay, day	6	1568/1117	-0.75[-1.26,-0.24] †	0.004	75.72	5	93%	<0.0001
Overall complications	14	2782/2767	0.50 [0.27, 0.92]	0.03	158.13	13	92%	<0.0001
Urinary continence-3mo	7	945/818	1.21[0.74,1.98]	0.45	13.33	6	55%	0.04
Urinary continence-12mo	4	942/1409	0.97[0.78,1.20]	0.79	10.89	6	45%	0.09
Potent recovery-3mo	4	722/685	4.50[1.91,10.62]	<0.001	17.64	3	83%	<0.001
Potent recovery-12mo	4	942/1409	1.58[1.05,2.36]	0.03	10.33	3	71%	0.02
Readmission rate	4	2850/3025	0.53[0.23,1.21]	0.13	24.10	3	88%	<0.001
Pathologic T stage								
≤pT2a	10	1725/1871	1.02[0.83,1.26]	0.83	7.02	9	0%	0.63
pT2b	9	1675/1821	0.99[0.80,1.21]	0.90	8.07	8	1%	0.43
≥pT2c	12	1979/2212	0.98[0.79,1.21]	0.84	9.48	11	0%	0.58
Pathological Gleason score								
≤6	27	5847/6576	0.99[0.87,1.13]	0.88	45.37	26	43%	0.01
7	27	5847/6576	1.14[1.02,1.28]	0.02	46.80	26	44%	0.007
≥8	27	5847/6576	0.79[0.67,0.92]	0.003	38.31	26	32%	0.06
PSM	39	13992/17806	0.87[0.76,0.99]	0.04	123.38	37	70%	<0.001
PSM for T2	16	6649/7986	0.71[0.53,0.95]	0.02	51.53	15	71%	<0.001
PSM for T3	12	1423/1713	1.39[1.19,1.63]	<0.001	9.38	11	0%	0.59
Mean lymph node yield	2	375/275	3.77[-5.87,13.41] †	0.44	106.54	1	99%	<0.001
Positive lymph node	10	2668/3684	0.69[0.52,0.90]	0.006	9.31	9	3%	0.41
BCR for free survival	5	1192/1797	1.16[0.71,1.89]	0.55	23.76	4	83%	<0.001

RARP=robot-assisted radical prostatectomy; RRP=retropubic radical prostatectomy; OR = odds ratio; WMD = weighted mean difference; CI = confidence interval.

0.04)(Figure 7). PSM rates in pT3 cancers was higher in RARP group (OR:1.46; 95% CI: 1.27 to 1.67; $P < 0.001$) (Figure 8). However, the results showed that PSM rates in pT2 cancers was lower in RARP (OR:0.77; 95% CI: 0.63 to 0.95; $P = 0.01$)(Figure 9). Four studies [20, 43, 60, 73] comparing mean lymph node yield and the results showed that lymph node yield is higher in RARP (WMD: 1.61; 95% CI: 1.18 to 2.05; $P < 0.001$)(Figure S9), and 16 studies [20, 26, 33, 34, 39, 49, 58, 61, 64-68, 73, 84, 85] reported on positive lymph node, There was a statistical differences decreased positive lymph node in RARP than RRP (OR:0.45; 95% CI: 0.31 to 0.65; $P < 0.001$)(Figure 10).

Outcomes of complications(Table 4)

Pooling data from 25 studies [9, 11, 17, 23, 24, 26, 27, 29, 31, 34, 35, 40, 42, 46, 48, 52-54, 59, 64, 72, 73, 80, 82, 84] reported on overall complications, RARP had lower overall complications in the RARP

than RRP(OR:0.43; 95% CI: 0.32 to 0.58; $P < 0.001$) (Figure 11). Next, a meticulous classification of overall complications showed that RRP had a higher incidence of rectal injury(OR:0.16; 95% CI: 0.07 to 0.39; $P < 0.001$) (Figure S10), pulmonary embolism(OR:0.47; 95% CI: 0.37 to 0.59; $P < 0.001$) (Figure S11), wound infections (OR:0.23; 95% CI: 0.11 to 0.46; $P < 0.001$) (Figure S12), bladder neck contracture(OR: 0.21; 95% CI: 0.08 to 0.60; $P = 0.003$) (Figure S13), urinary retention(OR:0.63; 95% CI: 0.47 to 0.84; $P = 0.002$)(Figure S14), deep venous thrombosis(OR:0.40; 95% CI: 0.25 to 0.66; $P < 0.001$) (Figure S15), urinary leakage(OR: 0.64; 95% CI: 0.58 to 0.70; $P < 0.001$) (Figure S16), lymphocele (OR:0.52; 95% CI: 0.29 to 0.94; $P = 0.03$) (Figure S17), and obturator nerve injury(OR:0.09; 95% CI: 0.01 to 0.75; $P = 0.03$) (Figure S18). There was no statistical differences between two groups in term of urinary tract infections(UTI) (OR:0.75; 95% CI: 0.37 to 1.54; $P = 0.44$)(Figure S19), ileus (OR:0.92; 95% CI: 0.56 to 1.51; $P = 0.73$) (Figure S20).

Urinary continence recovery and potent recovery (Table 4)

Pooling data of 9 studies [9, 21, 26, 50, 62, 70, 81, 83, 84] reported on 3-mo and 12-mo urinary continence

recovery between two groups. The forest plot showed that there were no statistical differences on the 3-mo and 12-mo urinary continence between two groups (3mo: OR:1.54; 95% CI: 0.92 to 2.58; $P = 0.10$; 12mo: OR:1.03; 95% CI: 0.84 to 1.27; $P = 0.75$, respectively)(Figure 12,

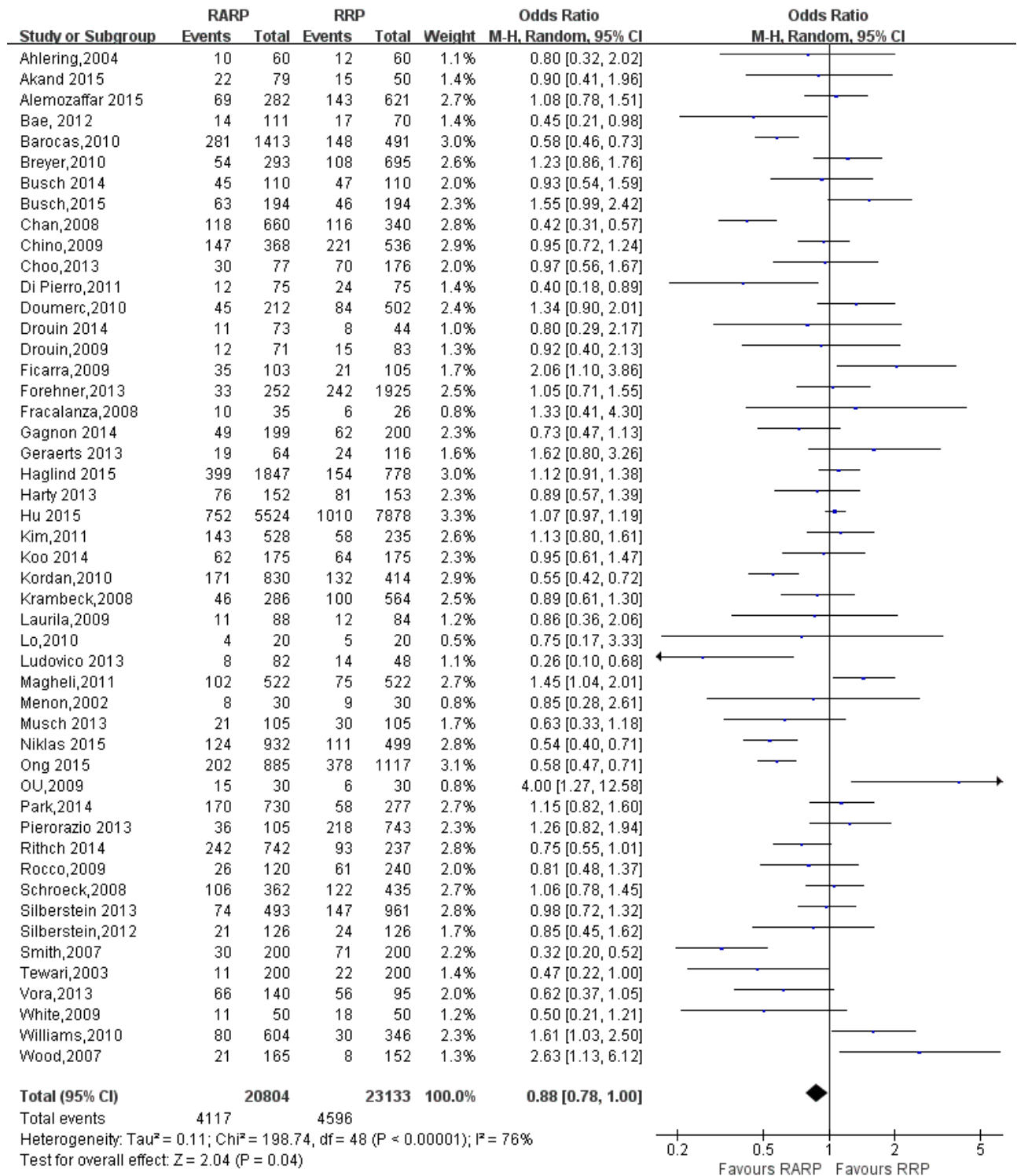


Figure 7: Forest plot and meta-analysis of PSM between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

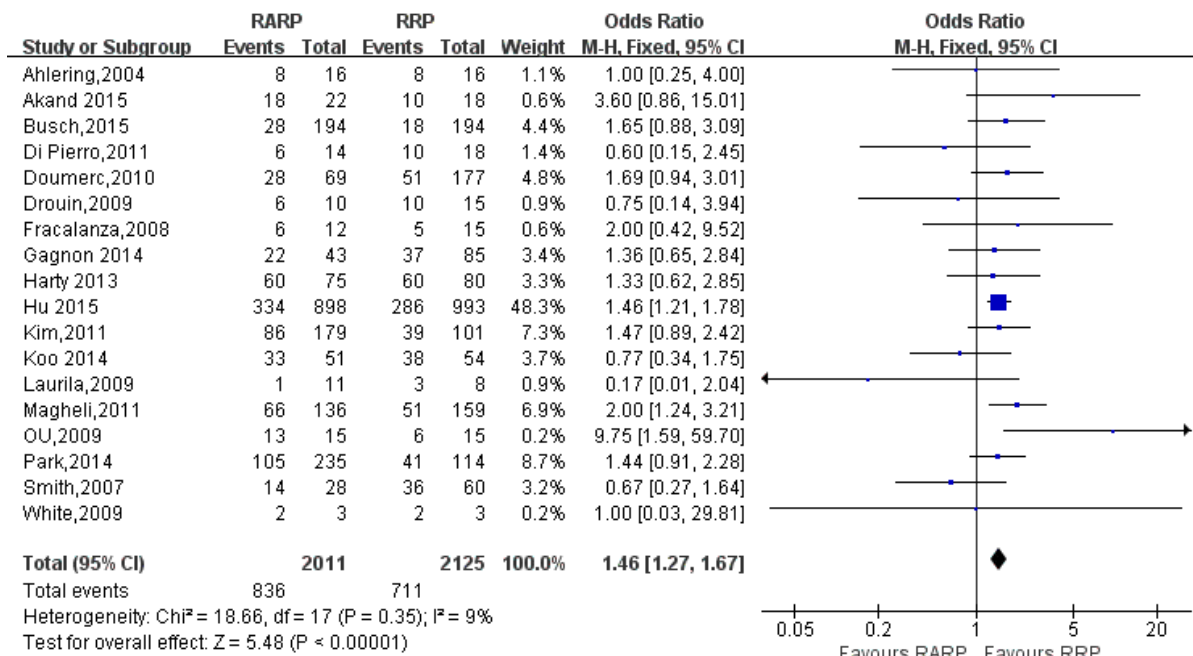


Figure 8: Forest plot and meta-analysis of PSM for pT3 between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

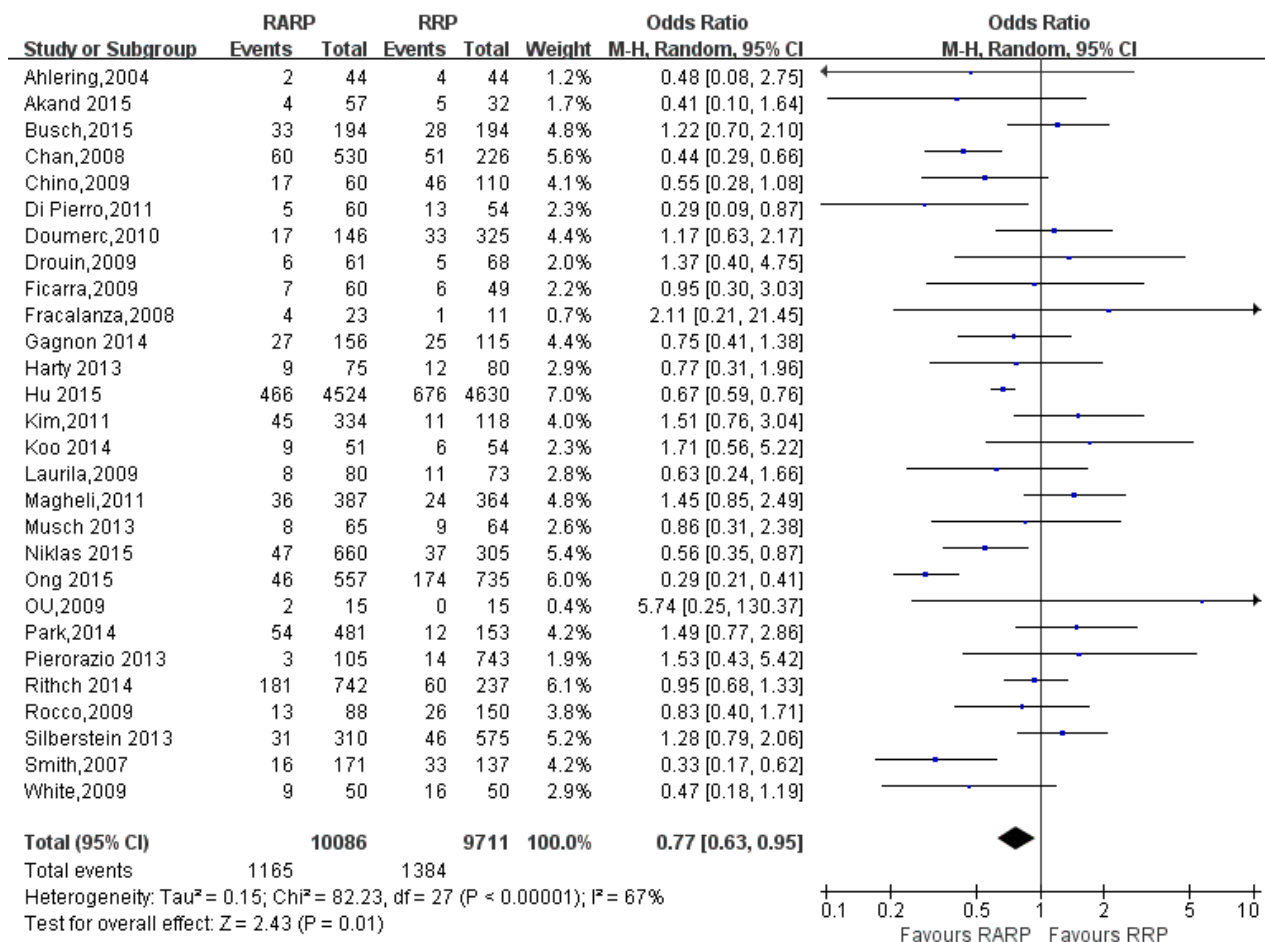


Figure 9: Forest plot and meta-analysis of PSM for pT2 between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

Figure S21). And the 3- and 12-mo potent recovery rate of RARP were better than RRP group, respectively (OR:3.19; 95% CI: 1.19 to 8.56; $P = 0.02$; OR: 2.37; 95% CI: 1.30 to 4.33; $P = 0.005$, respectively)(Figure 13,14).

Biochemical recurrence free survival and Readmission rate (Table 5)

Pooling data from 10 studies[12, 16, 34, 49, 56, 61, 65-67, 74] reported on biochemical recurrence(BCR) free survival, these results showed that RARP had a better BCR

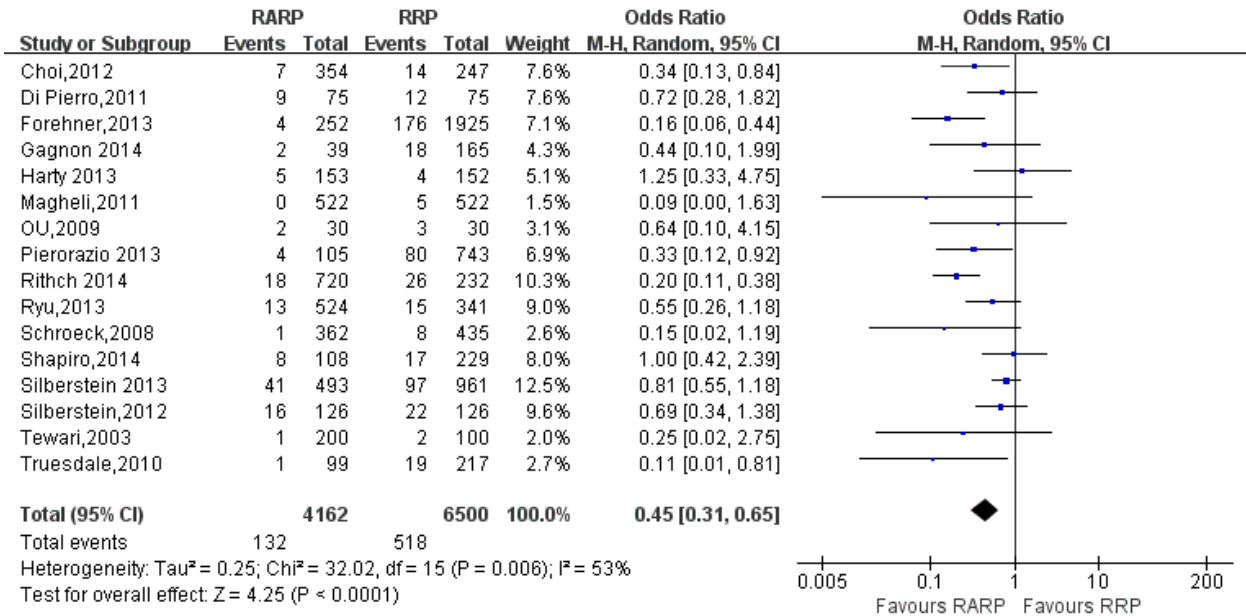


Figure 10: Forest plot and meta-analysis of positive lymph node between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

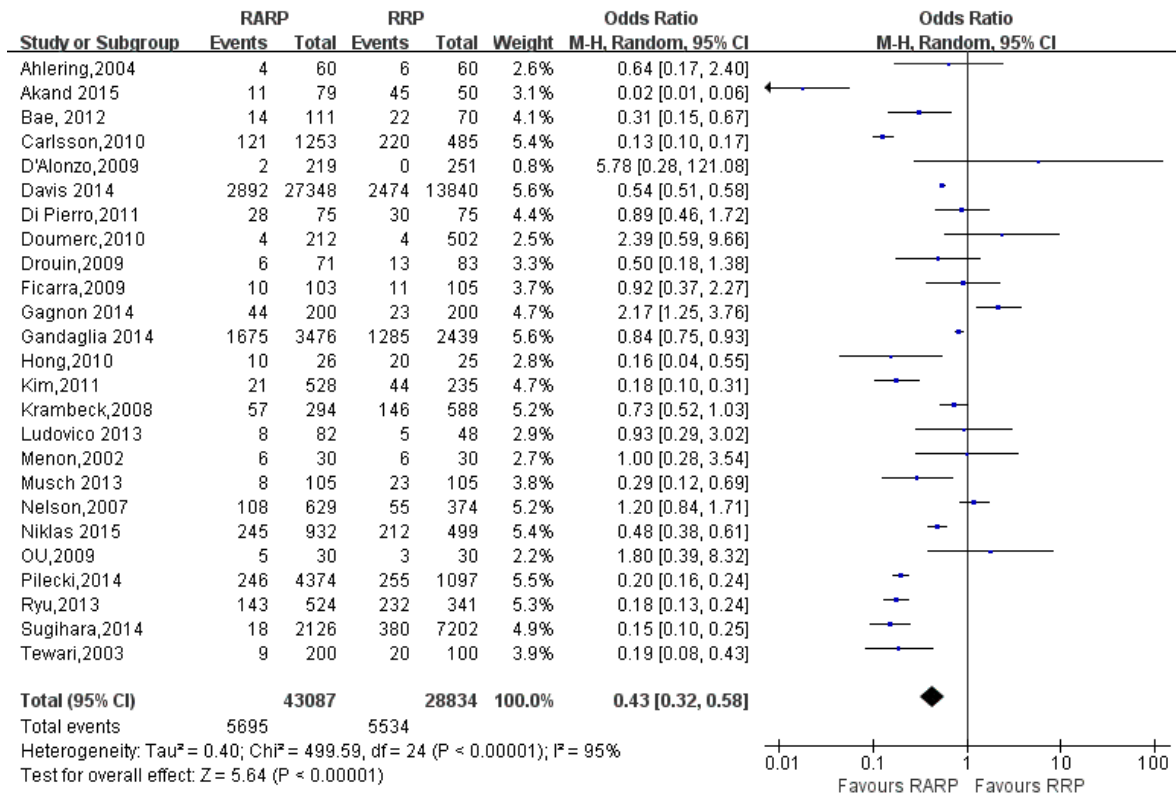


Figure 11: Forest plot and meta-analysis of overall complications between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

free survival than RRP(OR:1.33; 95% CI: 1.01 to 1.76; $P = 0.04$) (Figure 15). Pooling data from 7 studies[22, 35, 38, 53, 54, 59, 75] reported on readmission rate, the forest plot showed that RARP had a lower readmission rate than RRP(OR:0.83; 95% CI: 0.74 to 0.94; $P = 0.002$) (Figure 16).

Sensitivity analysis

42 qualified studies with patients' baseline characteristic consistency(age, pre-PSA, BMI, prostate volume, $P > 0.5$) are analyzed by sensitivity analysis (Table 6). Compared with the original analysis, there was no change in the significance of any other outcomes except that readmission rate($P = 0.002$ vs $P = 0.13$), and BCR for free survival($P = 0.04$ vs. $P = 0.55$) were significantly different in sensitivity analysis. The method of sensitivity analysis can reduce the heterogeneity of studies to a certain extent.

DISCUSSION

The incidence of prostate cancer and its mortality is the first and the second common cancer in man, respectively[1]. Our results indicated that RARP seemed to have an younger age (WMD: -1.00; $P < 0.001$), and to have the lower level of pre-PSA (WMD: -0.93; $P < 0.001$) than RRP group, and that these differences are primarily due to surgeon's preference for surgical modality. Another reason is that the younger is more easier to choose new approach. However, there is no difference on BMI and prostate volume between the two groups. Sensitivity analysis showed that there was no change in the significance of any other outcomes except that readmission rate($P = 0.002$ vs $P = 0.13$) and BCR for free survival($P = 0.04$ vs. $P = 0.55$).It demonstrated that selection bias of demographic and clinical data of patients is small between two groups.

Novara G et al[6] evaluated oncologic outcomes of RARP and RRP, and the results indicated that RARP had less EBL and transfusion rate than RRP. Their results presented similar results and strengthened our results. The

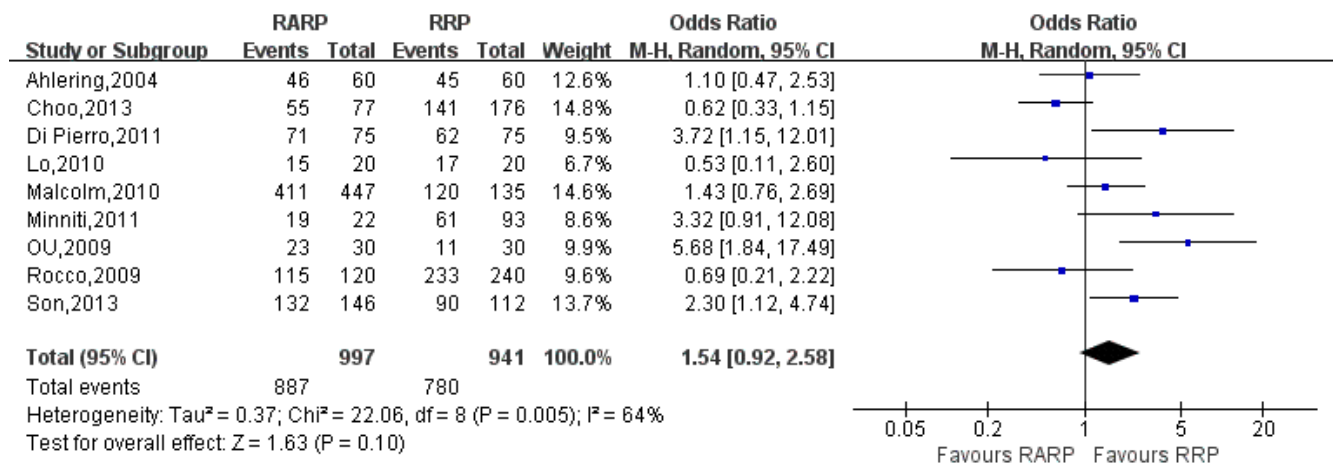


Figure 12: Forest plot and meta-analysis of 3-mo urinary continence rate between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

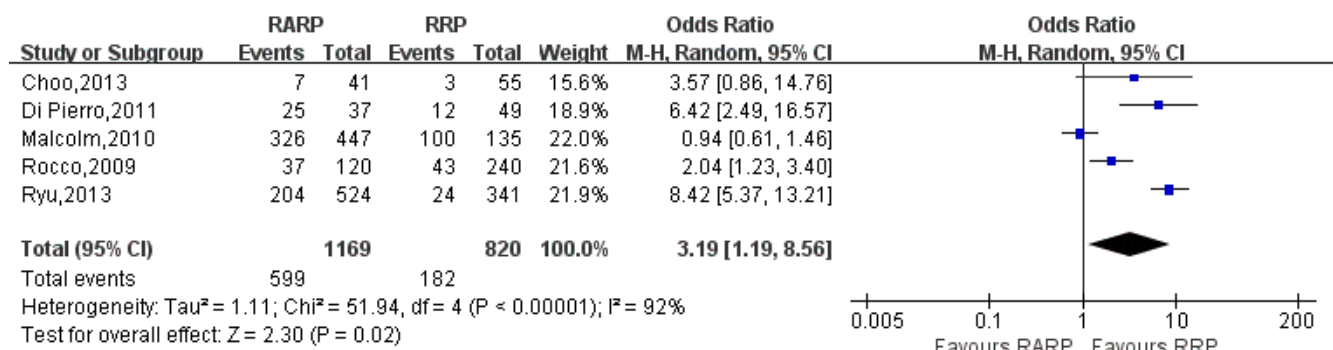


Figure 13: Forest plot and meta-analysis of 3-mo potent recovery rate between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

other analyzed parameters operative time and complication rate were similar. However, in our meta-analysis, RARP had longer operative time than RRP(WMD:39.85min, $P < 0.001$), which likely reflects the early learning curve with RARP. But the learning curve indicated that operative

time was decreased with growing operative experience and it won't influenced operative outcomes[88].

With regard to the pathologic outcomes, patients underwent RARP had more pathological Gleason score = 7, less pathological Gleason score ≥ 8 , higher lymph node

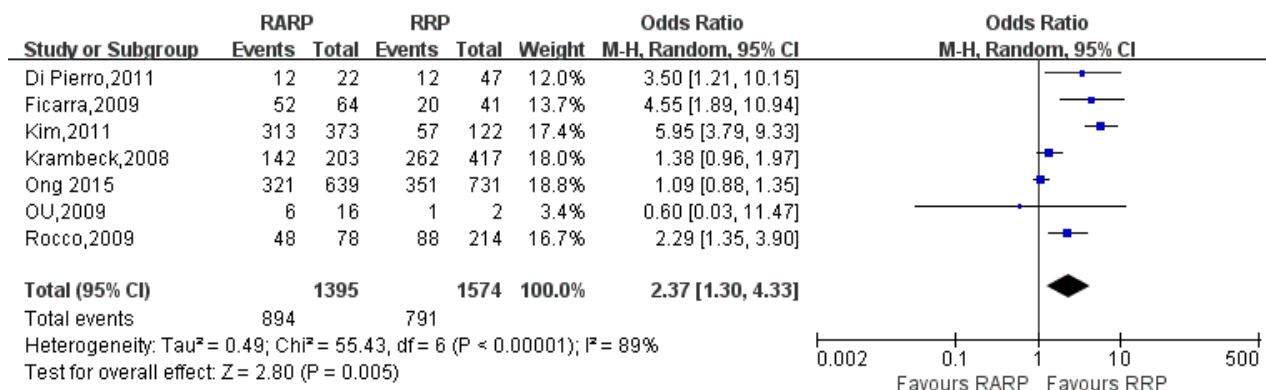


Figure 14: Forest plot and meta-analysis of 12-mo potent recovery rate between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

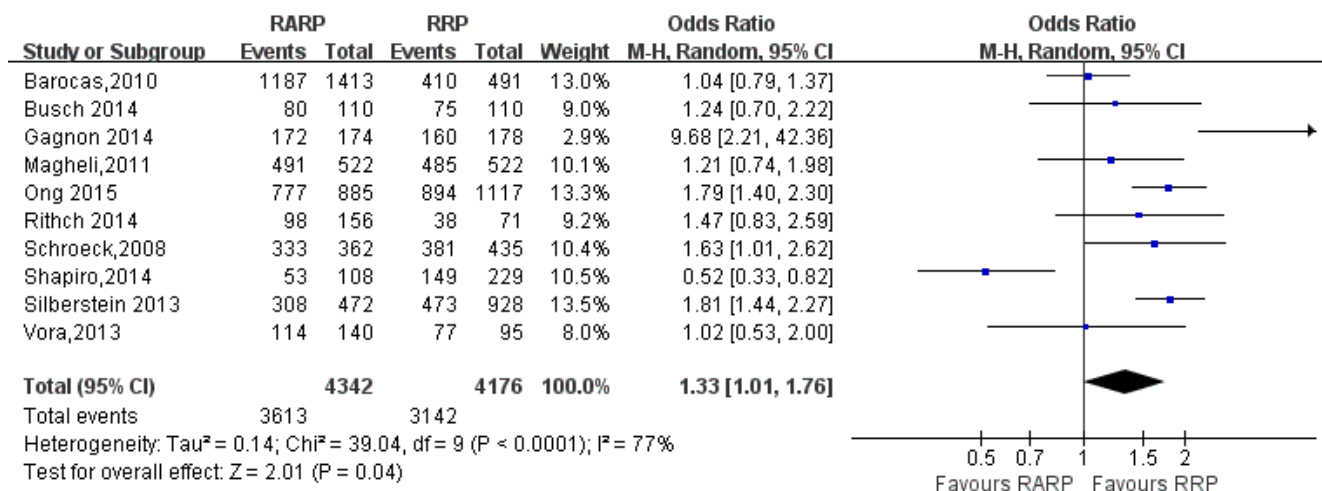


Figure 15: Forest plot and meta-analysis of BCR free survival rate between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

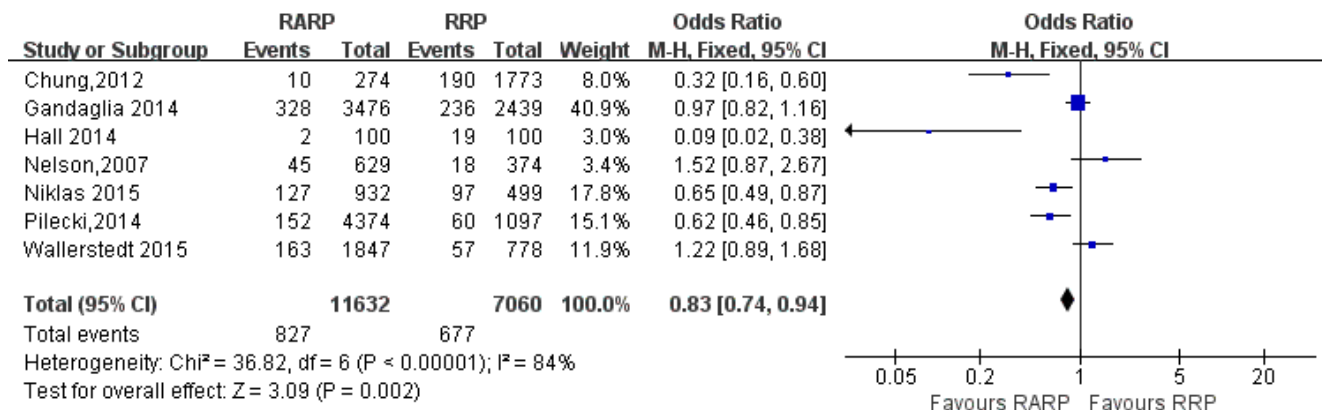


Figure 16: Forest plot and meta-analysis of readmission rate between RARP and RRP. RARP = robot-assisted radical prostatectomy; RRP = retropubic radical prostatectomy.

yield and fewer positive lymph node than RRP. However, the pathological T stage is no significant difference between the RARP and RRP group. LN yield was deemed an indicator of surgical quality by many surgeons[89]. RARP had a higher LN yield than RRP, the reason is that RARP has meticulous dissection with 3D vision and decrease the intraoperative blood loss which made the surgeon have more time and patience to acquiring higher LN yield. Therefore, the oncological outcomes in terms of PSM for T3 is higher in RARP than RRP. With the results that BCR free survival was higher in RARP than RRP. Some studies showed that the predictors of BCR were preoperative PSA, Gleason score, pathological stage, and PSM[49].

The experts suggested that patient outcomes and surgical approach were mainly required to improve for an accurate characterization of complications[90]. In our meta-analysis, Patients underwent RARP had fewer overall complications than RRP. The possible reason may be associated with lower EBL and less transfusion rate in RARP. Then a comprehensive classification of complications indicated that RRP had a higher incidence of rectal injury, pulmonary embolism, wound infections, bladder neck contracture, urinary retention, deep venous thrombosis, urinary leakage, lymphocele, and obturator nerve injury. There were no significant differences with regard to ileus and UTI between two groups.

Ficarra V et al[91] compared RARP with RRP with respect to 12-mo urinary continence. Their results indicated that RARP had a better 12-mo urinary continence recovery than RRP(OR:1.53; $P = 0.03$). However, our results indicated that there were no statistical differences with regard to 3-mo and 12-mo urinary continence in two groups. The urinary continence receiving RP is influenced by preoperative patient characteristics, surgical techniques, and so on. Some studies found that patient age[92, 93], BMI[94], comorbidity index[95], and prostate volume[96, 97] were also the potential predictors of urinary incontinence. Increasing age, higher BMI, and large prostate volume are correlated with high risk of urinary incontinence who underwent RP. However, the 3- and 12-mo potent recovery rate of RARP was also better than RRP group, respectively. Analysis of predictors indicated that peroperative parameters might influence potency results. Relevant predictors included age at surgery, baseline erectile function, and comorbidities[98]. Other authors also confirmed that age and baseline erectile function of patients were affected the potent recovery in nerve-sparing RARP[93, 99].

On the other hand, we found better BCR free survival and lower readmission rate in RARP group in the original analysis. The reason is that meticulous dissection, lower blood loss and complications might provide patients better oncologic prognosis in RARP group. However, we observed no statistical differences between RARP and RRP in sensitivity analysis. Therefore, multicenter, large

sample, long follow-up RCTs are required to prove our findings.

Nevertheless, there were several limitations when analyzing and interpreting results in our meta-analysis. The major limitation is lack of well designed prospective, randomized control studies in our meta-analysis. Secondly, there existed heterogeneities of studies, especially in the comparing of the continuous data such as the length of hospital stay, operative time. whereas these parameters were influenced by the heterogeneities of patients' conditions, surgeon's surgical skills and the sample size of studies. In addition, short follow-up duration may have an influence on the confidence of outcomes. In the future, well-designed, prospective, multicenter randomized control studies are required to help us better demonstrate the advantages as well as drawbacks of this novel approach.

MATERIALS AND METHODS

Literature search strategy

To update previous systematic review[5-7, 91, 98, 100, 101], a systematic review of published literature was performed according to the Cochrane Handbook recommendations[102]. No ethic issues get involved in this article. A systematic dissertation was conducted using Medline, Embase, Pubmed, CNKI, and all relevant studies had been identified by the Cochrane Library. The following key words were used: "comparative studies", "retropubic", "open", "radical prostatectomy", "Da Vinci", "robot-assisted", and "prostate cancer".

Data extraction and outcomes of interest

Two of the authors(JKH and TK) extracted data from the selected studies including: author identification, country, publication year, study design, age, No. of patients, operative approaches were mentioned previously, and results of intervention. All disagreements about eligibility were reached a consensus through authors discussion. Perioperative outcomes including operative time, EBL, LOS, overall complications, and oncological outcomes were compared between the two methods from all the studies that were finally selected. Overall complications were graded on the basis of the Clavien-Dindo system[103].

Inclusion criteria and exclusion criteria

Studies should satisfy the following requirements: (1) to compare RARP with RRP, (2) to display on outcome of two approaches, (3) to document the surgery

as RARP or RRP, (4) to clearly document indications for prostatectomy with prostate cancer. Studies will be excluded if (1) the study was not satisfied inclusion criteria or (2) the outcomes of literature were not mentioned or the parameters were impossible to analysis for either RARP or RRP from the published findings and (3) studies focusing on pure robot surgery system and/or on single-site techniques.

Study quality assessment and level of evidence

In accordance with the criteria of Centre for Evidence-Based Medicine in Oxford, we evaluated the level of evidence(LOE) of included sixteen studies. The Jaded Score was applied to evaluated the methodological quality of RCTs[104]. The Newcastle-Ottawa Scale(NOS) was applied to assessed the methodological quality of non-RCTs observational studies [86, 105]. Two authors(JKH and TK) evaluated the quality of the studies and discrepancies were rechecked by the third reviewer(CZQ) and consensus was achieved by discussion.

Statistical analysis

All meta-analysis were conducted by Review Manger 5.3(Cochrane Collaboration, Oxford, UK). Continuous and dichotomous variables were calculated by weighted mean differences (WMDs) and odds ratios(ORs). All analysis results were reported with 95% confidence intervals(CIs). I^2 test and chi-square-based Q test were applied to evaluated the quantity of heterogeneity, and when $I^2 > 50\%$, the evidence was considered to have substantial heterogeneity, the random-effects(RE) model would be applied, otherwise, the fixed effects(FE) model was applied. The presence of publication bias was evaluated by Egger's test and funnel plot. Sensitivity analysis was used to estimate the influence of studies with a high risk of bias on the overall effect.

CONFLICTS OF INTEREST

The authors have no conflict of interest to disclose.

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