

Impact of Pelvic Lymph Node Dissection and its Extension on Perioperative Complications and Morbidity in Patients with Prostate Cancer



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Introduction

- Pelvic lymph node dissection (PLND) plays a critical role in the staging and management of clinically localized prostate cancer
- Optimal extent of lymph node dissection not yet established
- Limited research exists relating extent of PLND and oncologic outcome
- European Association of Urology (EAU) recommends an extended approach for high-risk patients
- EAU defines "extended" PLND as removing lymph nodes adjacent to obturator nerve, internal, and external iliac vessels
- Goal of this study: to evaluate the difference in complication rates following standard vs. extended PLND

Methods

- Study design: systematic review and metanalysis in accordance with PRISMA guidelines
- Medline, Web of Science, Scopus, and Embase queried for papers
- Inclusion criteria:
 - Surgical series n >10
 - Non-oncologic intraoperative or postoperative complications as an outcome of interest
 - English language
- Standard vs. extended PLND assigned based on EAU definitions
- Patient demographics, quality of complication reporting, intraoperative, and postoperative complications recorded for each paper



- Initial search produced 3,645 papers
- 1,454 remained after removing duplicates
- 176 studies met inclusion criteria

Intraoperative Complications (IOC)

- 84 papers described IOC
 - 65 (77.4%) reported ≥1 IOC
 - Rate of IOC: 11.6% and strongly related to PLND extent
 - Rectal injury most common
 - IOC also included obturator nerve and iliac vessel
 injury

Postoperative Complications (POC)

- 151 papers analyzed POC
- 19 specially reported complication rates following standard vs. extended PLND
- 137 papers (90.7%) reported ≥1 POC
- Lymphatic system morbidities most common
- Lymphocele was the most frequently reported complication (90.6%) strongly related to PLND



Figure 2. Assessment of discrete categorization of perioperative complications of patients undergoing RP and PLND for prostate cancer. **a)** Intraoperative complications; **b)** Postoperative complications.

b) Likely PLND-re	elated Po	stope	rative Compli	cations	3		
	limited/star	ndard	extended/superex	tended		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
Kim et al., 2013	0	294	0	170		Not estimable	
Naselli et al., 2010	0	98	0	249		Not estimable	
Hoishi et al, 2015	0	599	0	131		Not estimable	
Allaf et al., 2004	0	1865	0	2135		Not estimable	
Liss et al., 2013	2	231	0	54	2.0%	1.19 [0.06, 24.34]	
Davis et al., 2011	0	261	3	670	2.1%	0.37 [0.02, 7.06]	
Jung et al., 2012	3	155	0	45	2.1%	2.06 [0.11, 39.24]	
Polcari et al., 2009	0	124	5	43	2.2%	0.03 [0.00, 0.57]	• • • • • • • • • • • • • • • • • • • •
Eden et al., 2010	2	253	1	121	2.9%	0.96 [0.09, 10.45]	
Altok et al, 2018	1	351	3	1239	3.1%	1.18 [0.12, 11.28]	
Clark et al., 2003	2	123	6	123	5.0%	0.33 [0.07, 1.62]	
Lindberg et al., 2009	2	64	8	108	5.2%	0.42 [0.09, 1.93]	
Mistretta et al., 2017	8	109	3	75	6.1%	1.83 [0.50, 6.69]	
Yun et al., 2013	11	204	3	202	6.2%	3.63 [1.03, 12.82]	
Briganti et al., 2006	4	196	19	767	7.1%	0.82 [0.28, 2.39]	
Eden et al., 2016	4	311	20	1000	7.1%	0.64 [0.22, 1.87]	
Heidenreich et al., 2002	8	100	6	103	7.3%	1.37 [0.49, 3.82]	
Katz et al, 2010	10	62	5	32	7.5%	1.03 [0.39, 2.76]	
Musch et al., 2008		867	16	434	8.0%	0.22 [0.09, 0.53]	
Morizane et al., 2018		902	28	431	8.3%	0.12[0.05, 0.27]	
Arenas et al., 2010	19	381	10	163	8.7%	0.81 [0.39, 1.71]	
Rievecka et al., 2007	28	740	13	230	9.2%	0.69 [0.36, 1.30]	
Total (95% CI)		8200		9531	100.0%	0.65 (0.41, 1.05)	
Total grants	110	02.50	140	0551	100.074	0.00 [0.41, 1.00]	· ·
Hotorogonoity Tout = 0.62	Chit= 41.0	0 dt = 17	149 /P = 0.0007); II = 61	0.94			
Test for merall effect: 7 - 1	1 77 (P = 0.09	0, ui = 17	(F = 0.0007), F = 0	5.10			0.005 0.1 1 10 200
restion overall effect. 2 -		"					Favours [limited/standard] Favours [extended/superextended]
c) Unlikely PLND-	related F						
-,,	-related F	ostop	perative Comp	olicatio	ns		
-,,	limited/sta	ndard	extended/supere	xtended	ns	Risk Ratio	Risk Ratio
Study or Subgroup	limited/sta Events	ndard Total	extended/supere Events	xtended Total	Weight	Risk Ratio M-H, Fixed, 95% Cl	Risk Ratio M-H, Fixed, 95% Cl
Study or Subgroup Polcari et al., 2009	limited/sta Events 0	ndard Total	extended/supere Events 0	xtended Total 43	Weight	Risk Ratio M-H, Fixed, 95% CI Not estimable	Risk Ratio M-H, Fixed, 95% Cl
Study or Subgroup Polcari et al., 2009 Naselli et al., 2010	limited/sta Events 0 0	ndard Total 124 98	extended/supere: Events 0 0	xtended Total 43 249	Weight	Risk Ratio M-H, Fixed, 95% Cl Not estimable Not estimable	Risk Ratio M-H, Fixed, 95% Cl
Study or Subgroup Polcari et al., 2009 Naselli et al., 2010 Musch et al., 2008	limited/sta Events 0 0 0	ndard Total 124 98 867	extended/supere: Events 0 0	xtended Total 43 249 434	Weight	Risk Ratio M-H, Fixed, 95% Cl Not estimable Not estimable Not estimable	Risk Ratio M-H, Fixed, 95% Cl
Study or Subgroup Polcari et al., 2009 Naselli et al., 2010 Musch et al., 2008 Allaf et al., 2004	limited/sta Events 0 0 0 0	124 98 867 1865	extended/supere: Events 0 0 0 0	xtended Total 43 249 434 2135	Weight	Risk Ratio M-H, Fixed, 95% Cl Not estimable Not estimable Not estimable Not estimable	Risk Ratio M-H, Fixed, 95% CI
Study or Subgroup Polcari et al., 2009 Naselli et al., 2010 Musch et al., 2008 Allaf et al., 2004 Clark et al., 2003	limited/sta Events 0 0 0 0 0	124 98 867 1865 123	extended/supere. Events 0 0 0 0 0	xtended Total 43 249 434 2135 123	Weight	Risk Ratio M-H, Fixed, 95% Cl Not estimable Not estimable Not estimable Not estimable	Risk Ratio M-H, Fixed, 95% CI
Study or Subgroup Polcari et al., 2009 Naselli et al., 2010 Musch et al., 2008 Allaf et al., 2004 Clark et al., 2003 Davis et al., 2011	limited/sta Events 0 0 0 0 0 0 0 0	124 98 867 1865 123 261	extended/supere Events 0 0 0 0 0 0 0 0 0	xtended Total 43 249 434 2135 123 670	Weight	Risk Ratio M-H, Fixed, 95% Cl Not estimable Not estimable Not estimable Not estimable Not estimable	Risk Ratio M-H, Fixed, 95% CI
Study or Subgroup Polcari et al., 2009 Naseili et al., 2010 Musch et al., 2008 Allaf et al., 2004 Clark et al., 2003 Davis et al., 2011 Hoishi et al., 2015	limited/sta Events 0 0 0 0 0 0 0 0 0 0	124 98 867 1865 123 261 599	extended/supere: Events 0 0 0 0 0 0 0 0 0 0 0 0 0 0	xtended Total 43 249 434 2135 123 670 131	Weight	Risk Ratio M-H, Fixed, 95% C1 Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable	Risk Ratio M.H. Freed, 85% CI
Study or Subgroup Polcari et al., 2009 Naselli et al., 2010 Musch et al., 2008 Allaf et al., 2004 Clark et al., 2004 Davis et al., 2011 Hoishi et al., 2015 Jung et al., 2012	limited/sta Events 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	124 98 867 1865 123 261 599 155	extended/supere: Events 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	xtended Total 43 249 434 2135 123 670 131 45	Weight	Risk Ratio M-H, Fixed, 95% CI Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable	Risk Ratio M-H, Fixed, 95% CI
Study or Subgroup Polcari et al., 2009 Naselli et al., 2010 Musch et al., 2008 Allaf et al., 2008 Clark et al., 2003 Davis et al., 2011 Hoishi et al., 2015 Jung et al., 2016 Altok et al., 2018	limited/sta Events 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	124 98 867 1865 123 261 599 155 351	extended/supere: Events 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	xtended Total 43 249 434 2135 123 670 131 45 1239	Weight	Risk Ratio M-H, Fixed, 95% CI Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable	Rusk Ratio M-H, Fixed, 95% CI
Study or Subgroup Polcari et al., 2009 Naselli et al., 2010 Musch et al., 2008 Allaf et al., 2003 Davis et al., 2011 Hoishi et al., 2011 Jung et al., 2012 Altok et al., 2018 Morizane et al., 2018	limited/sta Events 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	124 98 867 1865 123 261 599 155 351 902	extended/supere: Events 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	xtended Total 433 249 434 2135 123 670 131 455 1239 431	Weight	Risk Ratio M-H, Fixed, 95% Cl Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable	Risk Ratio M-II, Freed, 99% CI
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Study or Subgroup Polcan et al., 2009 Musch et al., 2010 Musch et al., 2010 Musch et al., 2008 Alfaf et al., 2008 Jung et al., 2010 Morzane et al., 2011 Morzane et al., 2011 Morzane et al., 2010 Morzane et al., 2010 Arenas et al., 2010 Lindberg et al., 2010 Misteffa et al., 2010 Misteffa et al., 2010 Misteffa et al., 2010 Misteffa et al., 2016 Misteffa et al., 2016	Inited/state Events 0	Indard Total 124 98 867 1865 123 261 599 155 351 902 294 231 64 740 109 100 311	extended/supere Events 0 0 0 0 0 0 0 0 0 0 0 0 0	Dicatio xtended Total 43 249 434 2135 1233 670 131 45 1239 431 170 54 121 163 2366 75 103 1000	0.9% 1.2% 2.0% 3.5% 5.5% 8.5% 9.6%	Risk Ratio M-4, Exed, 55% Cl Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable Not estimable 1.64 [0,21,13,02] 1.64 [0,21,13,02] 1.30 [0,01, 226] 0.64 [0,21,5,46] 0.13 [0,01, 226] 0.68 [0,39,190] 0.68 [0,39,190]	Risk Ratio M-J, Freed, USh Cl
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Figure 1. Intervention meta-analysis of studies comparing limited/standard PLND vs. extended/super-extended PLND. a) Strongly PLND-related postoperative complications; b) likely PLND-related postoperative complications c) Unlikely PLND-related postoperative complications

- Metanalysis demonstrated statistically significant decreased risk of complications with standard/limited PLND compared to extended/super-extended
 - IOC RR: 0.55 (p=0.01)
 - PLND-related POC RR: 0.55 (p=0.01)
- Extent of PLND is an independent predictor of lymphocele formation (RR:1.77; p>0.0001)

Conclusions

- Extended PLND may confer an oncologic benefit
- However, it is associated with an increased risk of intraoperative and postoperative complications, especially lymphocele formation
- Shared decision making must be undertaken between patient and practitioner when deciding extent of PLND