

## Research Communication

# Lymph swelling after radical prostatectomy and pelvic lymph node dissection

Guidelines recommend an extended pelvic lymph node dissection (ePLND) along with the radical prostatectomy (RP) if the estimated risk of lymph node (LN) metastases exceeds 5% [1]. Besides more accurate staging, the potential survival benefit of the LND is yet to be proven [2,3]. While women operated for cervical cancer with a similar ePLND template have a patient-reported occurrence of lymphoedema of ~35% [4], the staff-reported frequency of lymphoedema after RP ranges from 0% to 10% [5,6], and there is a need for better understanding of the trade-off between benefits and costs of the LND in prostate cancer.

We assessed the risk of groin and leg swelling after RP using patient-reported data within the prospective Laparoscopic Prostatectomy Robot Open (LAPPRO) trial [7]. We evaluated the effect of the extent of the LND, the surgical approach, and the surgeons' experience on the risk of groin and leg swelling, and to what extent any swelling impacts the quality of life.

The prospective controlled trial LAPPRO is a non-randomised multicentre trial including patients treated at 14 Swedish urological centers. We included patients aged <75 years who were operated for localised prostate cancer between 1 September 2008 and 7 November 2011. An ePLND was done according to the local criteria at the participating centers. The design and data collection of the LAPPRO trial have been described in detail previously [7].

The study patients completed validated questionnaires at 3, 12 and 24 months after surgery. We assessed the prevalence of patient-reported groin and leg swelling using the following questions at 3 months postoperatively: 'Have you had swelling in the left/right groin after surgery?', and 'Have you had swelling in the left/right leg after surgery?'. Patient-reported quality of life was evaluated using the following questions: 'How would you like to describe your quality of life in the past month?' and 'How do you rate your physical health in the past month?'. Staff-reported occurrence of swelling was assessed using the following questions recorded at 3, 12, and 24 months after surgery: 'Is there a swelling (sign of lymphoedema) in the groins?' and 'Is there a swelling (sign of lymphoedema) in the legs?'. We also used perioperative case report form (CRF) data to ascertain the following information: robot-assisted laparoscopic RP (RALP) or open surgical approach (retropubic RP [RRP]), extent of LND, and surgeons' experience. Data on LN yield was extracted from the pathology report.

We estimated crude and adjusted risks for different outcomes with multinomial logistic regression. The independent variables, all categorical, entered the regression models by means of indicator variables. The association of the outcome variables with the independent variables was summarised by relative risk ratios (RRs) with 95% CIs. We set the level of all our statistical tests at 5%. The analyses were performed with Stata statistical software, version 15 (StataCorp, College Station, TX, USA).

Out of 3675 men in the study, LND was done in 645 (17.6%; Table 1). At 3 months after RP, the prevalence of patient-reported moderate-to-severe swelling of the groin and leg was 13.7% (95% CI 11.1%–16.6%) among men who had undergone LND, compared with 3.0% (95% CI 2.5%–3.8%) among men who had not (Table 1). The staff-reported (CRF) prevalence of swellings was lower than the patient-reported, but repeated measurements over time indicates stable prevalence from 3 to 24 months after surgery.

The adjusted RR for the association between LND and moderate-to-severe swelling in the groin and legs at 3 months was 6.9 (95% CI 4.7–10.1; Table 2). Low surgical experience was not associated with reported swelling of the groin and leg, nor was there any clear difference between RALP and RRP (Table 2).

After adjusting for other side-effects, such as erectile dysfunction and incontinence, the adjusted relative risk for worst quality of life and physical health (patient-reported) was significantly increased among men with swelling of the groin or leg, or reported signs of swelling of groin and leg. This negative effect seemed to remain at 12 months after surgery, but decreased and was not statistically significant at 24 months postoperatively (Table 3).

We found a fourfold increased prevalence of patient-reported swelling in the groin and leg associated with the LND. Swelling symptoms remained at 12 and 24 months after surgery, and seemed to profoundly affect perceived physical health and quality of life. While staff-reported frequency of groin and leg swelling was 5%, 14% of our patients reported swellings at 3 months after surgery. Previous studies' findings of between 0% and 10% prevalence of swellings based on staff reports may likely have been underestimations.

We also found that swellings of the groin and leg negatively affect the patients' quality of life and physical health. Swelling after LND has been carefully studied and recognised in breast

**Table 1** Postoperative lymph swelling after RP in relation to LND, surgical experience, and surgical technique.

Swelling of groin or leg at 3 months after RP	Patient-reported			Doctor-reported					
	3 months			6–12 weeks		12 months		24 months	
	N (%)	Little, n (%)	Moderate/much, n (%)	No, n (%)	Yes, n (%)	No, n (%)	Yes, n (%)	No, n (%)	Yes, n (%)
LND <sup>a</sup>									
Yes	437 (70.4)	99 (16.0)	85 (13.7)	584 (94.8)	32 (5.2)	380 (95.7)	17 (4.3)	300 (95.5)	14 (4.5)
No	2578 (88.8)	235 (8.1)	89 (3.0)	2921 (99.5)	15 (0.5)	1910 (98.8)	24 (1.2)	1431 (98.6)	21 (1.4)
LND <sup>a</sup>									
Limited	208 (74.6)	39 (14.0)	32 (11.5)	269 (97.5)	7 (2.5)	182 (98.4)	3 (1.6)	139 (97.9)	3 (2.1)
Extensive	213 (65.3)	60 (18.4)	53 (16.3)	300 (92.3)	25 (7.7)	185 (92.7)	14 (7.0)	150 (93.2)	11 (6.8)
LN yield <sup>b</sup>									
1–4	47 (79.7)	10 (16.7)	2 (3.4)	60 (100)	0 (0)	35 (100)	0 (0)	26 (100)	0 (0)
5–9	70 (68.6)	17 (16.7)	15 (14.7)	97 (93.3)	7 (6.7)	68 (95.8)	3 (4.2)	46 (95.8)	2 (4.2)
10–19	93 (62.8)	23 (15.5)	32 (21.6)	133 (90.5)	14 (9.5)	75 (92.6)	6 (7.4)	68 (91.9)	6 (8.1)
≥20	94 (69.1)	25 (18.4)	17 (12.5)	132 (93.6)	9 (6.4)	74 (92.5)	6 (7.5)	47 (92.2)	4 (7.8)
Surgeon experience <sup>a</sup>									
<50	398 (87.0)	36 (7.9)	23 (5.0)	448 (98.7)	6 (1.3)	289 (98.6)	4 (1.4)	189 (98.4)	3 (1.6)
<100	417 (87.8)	40 (8.4)	18 (3.8)	476 (98.7)	5 (1.0)	283 (99.0)	3 (1.0)	187 (98.4)	3 (1.6)
<200	790 (84.3)	92 (9.8)	55 (5.9)	962 (98.9)	11 (1.1)	552 (97.7)	13 (2.3)	391 (98.0)	8 (2.0)
≥200	1396 (85.1)	165 (10.0)	80 (4.9)	1604 (98.5)	25 (1.5)	1162 (98.2)	21 (1.8)	961 (97.9)	21 (2.1)
RRP	729 (80.7)	118 (13.0)	56 (6.2)	858 (98.4)	14 (1.6)	654 (97.9)	14 (2.1)	527 (97.8)	12 (2.2)
RALP	2309 (87.1)	220 (8.3)	122 (4.6)	2663 (98.7)	34 (1.3)	1650 (98.5)	27 (1.6)	1217 (98.2)	23 (1.8)

Abbreviations: RALP, robot-assisted laparoscopic RP; RRP, retropubic RP. <sup>a</sup>As defined at operation by surgeon. <sup>b</sup>As described in pathology report.

**Table 2** Risk factors for lymph swelling after RP.

a	Patient-reported				Doctor-reported							
	3 months				6–12 weeks		12 months		24 months			
	Little swelling		Moderate/much swelling									
	Adj RR <sup>b</sup> (95% CI)	P	Adj RR <sup>b</sup> (95% CI)	P	Adj RR <sup>b</sup> (95% CI)	P	Adj RR <sup>b</sup> (95% CI)	P	Adj RR <sup>b</sup> (95% CI)	P	Adj RR <sup>b</sup> (95% CI)	P
LND												
Yes vs no	3.1 (2.3–4.1)	<0.001	6.9 (4.7–10.0)	<0.001	LND							
Ext. vs lim.	1.6 (0.95–2.7)	0.075	1.2 (0.7–2.1)	0.44	Yes vs no	14.1 (6.5–30.5)	<0.001	3.7 (1.8–7.7)	<0.001	2.7 (1.2–6.3)	0.014	
LN yield					Ext. vs lim.	2.2 (0.9–5.5)	0.094	3.5 (0.9–13.3)	0.94	3.4 (0.6–19.0)	0.16	
1–4	1 (ref)	1 (ref)	1 (ref)		LN yield	1.3 (0.9–1.8)	0.35	1.4 (0.7–2.7)	0.28	0.9 (0.3–2.3)	0.82	
5–9	0.8 (0.27–2.2)	0.63	3.8 (0.79–18.6)	0.096	Surgical experience							
10–19	0.9 (0.35–2.3)	0.84	5.7 (1.2–26.5)	0.025	<50	1 (ref)	0.15	1 (ref)	0.12	1 (ref)	0.34	
≥20	1.0 (0.39–2.5)	0.98	2.9 (0.61–14.3)	0.178	<100	1.5 (0.35–6.4)		1.4 (0.24–8.7)		0.95 (0.13–6.9)		
Surgical experience					<200	1.25 (0.33–4.8)		2.8 (0.62–13.0)		1.55 (0.32–7.5)		
<50	1 (ref)				≥200	2.24 (0.65–7.7)		2.7 (0.62–12.0)		1.74 (0.39–7.8)		
<100	1.3 (0.76–2.3)	0.33	0.99 (0.49–2.0)	0.98	RALP vs RRP <sup>b</sup>	0.7 (0.3–1.5)	0.34	0.7 (0.3–1.4)	0.28	0.9 (0.4–2.3)	0.86	
<200	1.4 (0.85–2.3)	0.19	1.4 (0.79–2.6)	0.24								
≥200	1.6 (0.99–2.5)	0.056	1.2 (0.66–2.1)	0.57								
RALP vs RRP <sup>c</sup>	1.2 (0.60–2.51)	0.57	0.9 (0.44–1.87)	0.79								

Abbreviations: Adj., adjusted; Ext., extensive; lim., limited. <sup>a</sup>'No swelling' group was reference category, and was omitted. <sup>b</sup>Adjusted for diabetes, smoking, re-operation, complications, hernia, body mass index, and age. <sup>c</sup>In addition adjusted for LN yield.

cancer [8] and gynaecological cancers, but the condition has received less attention in the context of prostate cancer, despite the fact that the template of the LND is similar to that of several gynaecological cancers. We recommend future studies to confirm our findings using patient-reported measures.

We could not find any correlation between the number of LNs removed and swelling of the groin and leg. However, we found that removal of only one to four LNs compared with

≥10 was associated with a statistically significant difference in swelling. The risk of swelling in the groin/legs was non-significantly increased after extended LND compared with limited LND, but the variation in reported number of LNs from different pathologists may have attenuated this comparison.

The LAPPRO trial is one of the largest and most valid population-based comparisons of RALP and open RRP.

**Table 3** Quality of life in relation to postoperative lymph swelling after RP.

Patient-reported	No, n (%)	Little, n (%)	Moderate/much, n (%)	RR	P	RR <sup>a</sup> (95% CI)	P
3 months							
Quality of life							
Good	1426 (47.2)	128 (38.0)	60 (33.7)	1 (ref)		1 (ref)	
Medium	1392 (46.0)	177 (52.5)	99 (55.6)	1.3	<0.001	1.4 (1.2–1.6)	<0.001
Worse	207 (6.8)	32 (9.5)	19 (10.7)	1.5	<0.001	1.6 (1.2–2.0)	<0.001
Physical health							
Good	1678 (55.4)	152 (45.1)	57 (32.2)	1 (ref)		1 (ref)	
Medium	1217 (40.1)	158 (46.9)	94 (53.1)	1.5	<0.001	1.6 (1.3–1.8)	<0.001
Worse	135 (4.5)	27 (8.2)	26 (14.7)	2.3	<0.001	2.2 (1.7–2.9)	<0.001
Doctor-reported	No, n (%)	Yes, n (%)	RR	P	RR <sup>a</sup> (95% CI)	P	
12 months							
Quality of life							
Good	1248 (57.8)	14 (37.8)	1 (ref)		1 (ref)		
Medium	821 (38.0)	18 (48.7)	1.9	0.062	1.6 (0.7–3.4)	0.23	
Worse	92 (4.2)	5 (13.5)	4.8	0.003	5.7 (1.9–16.4)	0.002	
Physical health							
Good	1275 (58.1)	12 (31.6)	1 (ref)		1 (ref)		
Medium	817 (37.7)	24 (63.2)	3.1	0.001	2.9 (1.4–6.0)	0.006	
Worse	76 (3.5)	2 (5.3)	2.7	0.18	3.3 (0.7–14.7)	0.15	
24 months							
Quality of life							
Good	925 (54.4)	20 (48.6)	1 (ref)		1 (ref)		
Medium	680 (42.0)	16 (45.7)	1.4	0.33	1.4 (0.7–2.9)	0.37	
Worse	59 (3.6)	2 (5.7)	1.5	0.59	0.8 (0.1–6.1)	0.83	
Physical health							
Good	880 (61.3)	20 (57.1)	1 (ref)		1 (ref)		
Medium	971 (35.5)	12 (34.3)	0.8	0.49	0.7 (0.3–1.5)	0.36	
Worse	88 (3.2)	3 (8.6)	2.4	0.20	2.7 (0.8–9.7)	0.12	



<sup>a</sup>Adjusted for age, body mass index, erectile dysfunction, and incontinence.

Our use of patient-reported symptoms is a clear strength in this present analysis. Apart from the non-randomised design, the main limitation of the study is that the patient-reported questions on swelling at 3 months were not repeated in subsequent follow-up questionnaires at 12 and 24 months.

In summary, LND during RP was associated with an elevated risk of persisting lymph swelling postoperatively and impacted negatively the quality of life of the patients. These findings suggest that patients should be explicitly informed about lymph swelling as a potentially persisting side-effect. The frequent occurrence of lymph swelling emphasises the need for careful consideration of risks vs potential benefits, and the need for randomised studies evaluating whether or not surgical removal of the LNs entails any important benefit beyond disease staging.

## Conflict of Interest

None declared.

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Abbreviations: CRF, case report form; (e)(P)LND, (extended) (pelvic) lymph node dissection; LAPPRO, Laparoscopic Prostatectomy Robot Open; LN, lymph node; RALP, robot-assisted laparoscopic RP; (R)RP, (retroperitoneal) radical prostatectomy; RR, risk ratio.